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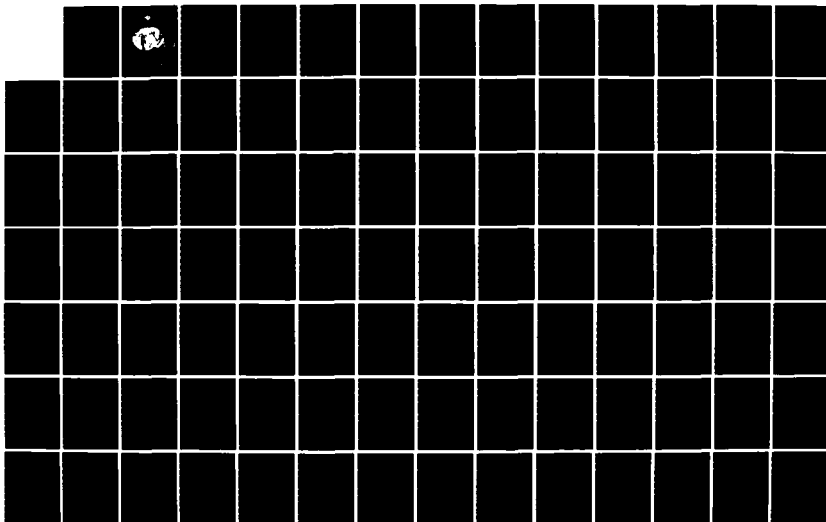
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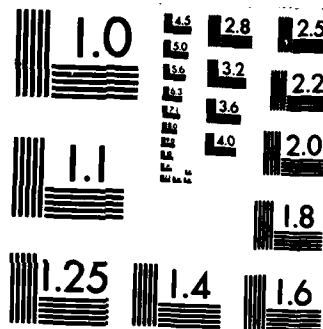
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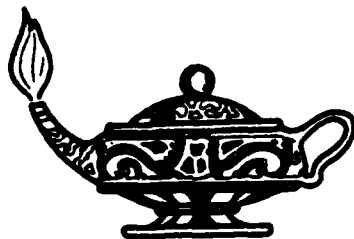
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EL PASO, TEXAS 79920

CLINICAL INVESTIGATION PROGRAM
RCS MED-300 (R1)

FY 84 ANNUAL PROGRESS REPORT

This report was prepared under the direction of COL M.R. Weir,
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) This report serves to detail the progress, status, and funding of approved projects conducted under protocol by staff members, interns, and residents at William Beaumont Army Medical Center. The varying projects as reported are classified according to the service or department to which the principal investigator belongs. Research conducted at WBAMC is categorized as either basic experimental medicine or trials and testing of clinical medicine procedures using the indigenous population for which this medical facility provides support. Medical departments involved in this program include		

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FOREWORD

As a new chief in the Department of Clinical Investigation (DCI), it seems appropriate to outline my concept of the role of DCI. That role follows from the purpose, which is to enhance understanding of medical developments and the medical literature by fellows and house officers. The role begins with an idea and progresses to a publication. The process has seven steps:

1. The idea for research is transformed to a project.
2. The project generates a protocol.
3. The protocol progresses through the approval process.
4. Special laboratory testing or use of animal models are employed.
5. Data is accumulated, analyzed and interpreted.
6. Statistical support may be required.
7. The manuscript is prepared and submitted.

This process, though a bit mechanical, provides the opportunity to be creative. For many potential researchers the process appears long and they must be introduced slowly by a mentor. The ideas of a new investigator may first appear as a case report or series of cases. The process and the paper encourage the investigator to do a retrospective review, a prospective project, followed by an intervention study, and the process is complete. In addition, there may be a judgment call by the mentor (C, DCI or department staff) about the present state of the potential researcher. He may need a gentle nudge to go a bit beyond his current capabilities.

The seven basic steps require some elaboration. DCI becomes involved in expanding the idea to a project. The idea is analogous to a goal, which is important, grandiose, vague and untestable. The project corresponds to an objective, a narrowing of the idea to include some measurable element or parameter. Frequently a variety of measurable elements are necessary because the principal idea cannot be supported by the measured results. Instead, some other, unexpected relationship is demonstrated, altering the concept. The idea is modified by the failure to demonstrate the anticipated results or the serendipitous positive findings.

Progressing from project to protocol is basically a series of technical maneuvers requiring advisory guidance from DCI to include changes, as dictated by the most recent regulatory and political forces. Following protocol approval, DCI may be asked for special laboratory tests, animal model support, or both.

Data accumulation, management and analysis follow, frequently requiring statistical support beyond the capability of most physicians. Very elaborate data support and statistics requiring large computers may be required.

Finally, the abstract presentation and publication preparation phase ensue. This phase may involve DCI for concepts, technical guidance, etc. This is the act of encouraging research and publication in the mind of this new chief.

Acknowledgments: This volume's existence owes much to LTC Lyndon E. Mansfield, M.D., who was Chief, DCI, for the 83-84 academic year, who laid in place many of the plans I enjoyed seeing come to fruition; BG John E. Major, an advocate of the role of clinical investigation; and Peggy Casteel, whose tireless efforts got the document to the printer. It further acknowledges the contribution of those who departed during the FY: MAJ A. W. O'Brien, DVM, who headed the Biological Research Service for three years; Robert J. Frederick, PhD, who headed the Microbiology Service for six years; and finally, a number of colleagues on the WBAMC staff who contributed their time and that of their residents for research and publication efforts.



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DEPARTMENT OF DENTISTRY

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Housing T: Chinese-American cultural health beliefs, practices and healers. 6th Bi-National Nursing Conference, Transcultural Nursing Council, El Paso, TX, Mar 1984.

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Mika W: German-American cultural health beliefs, practices, and healers. 6th Bi-National Nursing Conference. Transcultural Nursing Council, El Paso, TX, Mar 1984.

Mika W: Role of the health clinic head nurse: An euphermistical, critical and analytical study. Shea-Arentzen Nursing Symposium, San Diego, CA, May 1984.

Mitman-Montano M: Cystic Fibrosis. 2nd Annual Nursing Care of the Criticall Ill Child Workshop, El Paso, TX, May 1984.

Odom J: Pathophysiology of the beta-adrenergic theory and effects of drugs. 2nd Annual Nursing Care Conference, WBAMC, El Paso, TX, Apr 1984.

*Odom J: Evaluation of post-partum and infant care teaching program at WBAMC. Phyllis J. Verhonick Research Symposium, Washington, DC, Sep 1984.

Odom J: Environmental variables and acute asthmatic attacks in children. Phyllis J. Verhonick Research Symposium, Washington, DC, Sep 1984.

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Parry B: Physical and behavioral indicators of the sexually abused child. Child Abuse Conference, El Paso, TX, Jan 1984.

Parry B: Abuse: Recognition-intervention-prevention. Child Abuse Conference, El Paso, TX, Jan 1984.

Parry B: Victims of child sexual abuse. Texas Conference on Child Abuse and Neglect, El Paso, TX, Feb 1984.

Parry B: Victims of child sexual abuse. Texas Conference on Child Abuse and Neglect. Edinburg, TX, Mar 1984.

Parry B: Seizures. Special Olympics Training Workshop, El Paso, TX, May 1984.

Parry B: Prevention of child sexual victimization. ASTAC Annual Conference, Santa Fe, NM, May 1984.

Parry B: Meningitis. 2nd Annual Nursing Care of the Critically Ill Child Workshop, El Paso, TX, May 1984.

Parry B: Child sexual abuse: Educating the public. AASECT/SSSS National Conference, Boston, MA, Jun 1984.

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DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

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Hill PS, Weisman I.: Sarcoidosis and pregnancy. Case review. Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

Low ND, Theard FC: Postpartum cardiomyopathy: A rare phenomenon? Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

Low ND, Miles PA, Greenberg H: Multifocal microinvasive squamous cell carcinoma of the vulva - a rare entity: A case report of three separate foci of microinvasion. Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

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Stock RJ: Ectopic pregnancy after tubal ligation: What to ask; what to look for. Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

Stock RJ: An evaluation of possible sequelae of tubal ligation: An analysis of 75 consecutive hysterectomies. Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

Stock RJ: Rupture of the uterus following classical Cesarean section. Presented at the Armed Forces District, American College of Obstetricians and Gynecologists, Las Vegas, NV, Oct 1983.

Stock RJ: Sin revisited. Presented at the Armed Forces District, American College Obstetricians Gynecologists, Las Vegas, NV, Oct 1983.

DEPARTMENT OF PATHOLOGY

Pittman DL, Parker A: Immunologic marker studies on endoscopically obtained biopsies of gastric lymphoma. Presented at a workshop at SFAMLS 7th Annual Meeting, Washington, DC, Mar 1984.

DEPARTMENT OF PEDIATRICS

Kossoy AF, Weir MR: Conservative management of asymptomatic patients with elevated alcohol, carbamazepine, theophylline, and thyroxin levels. Poster presentation at the Uniformed Services Section of the American Academy of Pediatrics Fall Meeting, San Francisco, CA, Oct 1983.

Lampe RM, Weir, MR, Weeks J: Measles reimmunization in children immunized before one year of age. Poster presentation at Uniformed Services Section of the American Academy of Pediatrics Fall Meeting, San Francisco, CA, Oct 1983.

Lampe RM, Schydlower M, Collantes M, Lawson M: Non-group A beta hemolytic streptococcal pharyngitis among adolescents. Poster presentation at Uniformed Services Section of the American Academy of Pediatrics Fall Meeting, San Francisco, CA, Oct 1983.

Lampe RM, Weir MR: Erythromycin versus sulfisoxazole prophylaxis for recurrent otitis media. Presented at the Uniformed Services Pediatric Seminar, Reno, NV, Mar 1984.

Lampe RM, Schydlower M, Collantes M, Lawson M: Non-group A beta hemolytic streptococcal pharyngitis among adolescents. Poster presentation at American Academy of Pediatrics Spring Meeting, Phoenix, AZ, Apr 1984.

Schydlower M, Butler A, Scott RM, Rawlings P: Adolescent immunity to measles and outbreak control. Poster presentation at Uniformed Services Section of the American Academy of Pediatrics Fall Meeting, San Francisco, CA, Oct 1983.

Schydlower M: Adolescent respiratory illness. Presented at McAfee Health Clinic, White Sands Missile Range, NM, 8 Mar 1984.

Stafford W, Mena H, Piskun W, Weir M: Transverse myelitis due to intra-arterial penicillin. Poster exhibit at the 1983 Neurosurgery Conference, Chicago, IL, Nov 1983.

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Weir MR, Gwinn JV, Fearnow RG: Pediatric intern orientation. Poster presentation at Uniformed Services Section of the American Academy of Pediatrics Fall Meeting, San Francisco, CA, Oct 1983.

*Weir MR, Lampe RM, Schydlower M: Beyond visual otoscopy: New technology in the diagnosis of otitis media. Scientific Exhibit (Gold Medal Teaching Award) at the Amer Acad Pediatrics Meeting, Chicago, IL, Sep 1984.

DEPARTMENT OF PSYCHIATRY

Jeffrey LK, Jeffrey TB: Exclusion therapy in the treatment of smoking cessation. Presented at the Annual Scientific Meeting of the American Society of Clinical Hypnosis, 1984.

DEPARTMENT OF SURGERY

Apgar RG: The WBAMC experience with carcinoid tumors of the gastrointestinal tract. Presented at the Amer College of Surgeons, New Mexico Chapter, Las Cruces, NM, Jun 1984.

Cabellon S: Vascular injuries in the neck. Presented at the Amer College of Surgeons, New Mexico Chapter, Las Cruces, NM, Jun 1984.

Cavanaugh DG: Ten year experience with esophageal cancer at WBAMC. Presented at the Amer College of Surgeons, New Mexico Chapter, Las Cruces, NM, Jun 1984.

Cavanaugh DG: Thoracotomy in neck injuries. Presented at the Trauma Symposium, El Paso, TX, Nov 1983.

Cleland B: Emergency abdominal surgery in the aged. Presented at the Amer College of Surgeons, New Mexico Chapter, Las Cruces, NM, Jun 1984.

Oliphant JR: External ear injuries intratemporal facial nerve injury. Presented at the 3d Annual Trauma Symposium, El Paso, TX, Nov 1983.

Piskun W: CNS considerations in head and neck injuries. Presented at the Trauma Symposium, El Paso, TX, Nov 1983.

Theisen F: Mandibular fractures. Presented at the 3d Annual Trauma Symposium, El Paso, TX, Nov 1983.

Todhunter W: The treatment of biliary obstruction by U-tube or percutaneous transhepatic catheter drainage. Presented at the American College of Surgeons, New Mexico Chapter, Annual Meeting, Las Cruces, NM, Jun 1984.

UNIT SUMMARY

OBJECTIVES

If the goal of DCI is to further enhance fellow's and resident's ability to evaluate medical advancement and the literature as its report, the objectives appear to be more papers, more protocols, and more research; in this case with less money and no additional personnel. Realistically, the objective must be continued support of residencies and fellowships, resulting in higher quality research and publications. Since one cannot match or exceed previous productivity year after year, a unit objective of protocol and paper production that is 70-80% of the running average of three previous years is reasonable and measurable. We met this objective.

TECHNICAL APPROACH

The Department of Clinical Investigation provides support for staff and housestaff research projects under the guidelines of the Declaration of Helsinki, Clinical Investigation Program (AR 40-38), HSC Reg 40-23, and the Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances (AR 40-7). Research is conducted under protocols approved by the Research Committee (WBAMC HR 15-1), the Human Use Committee (WBAMC HR 15-1) and the Radioisotope Committee (WBAMC HR 15-1) where applicable. In those research protocols utilizing laboratory animals, the Animal Use Committee ensures that the investigators follow guidelines set forth in "Guide for Laboratory Animal Facilities and Care," published by the National Academy of Sciences-National Research Council, and the criteria established by the American Association for Accreditation of Laboratory Animal Care.

PERSONNEL

FY84 saw the departure of three key personnel of the four that head the department and the three services. All have been replaced early in the new fiscal year, but only time will tell that the impact of this turmoil has been overcome. LTC Lyndon E. Mansfield, MC, moved to private practice in El Paso. Robert J. Frederick, PhD, took a position at the Environmental Protection Agency. MAJ A.W. O'Brien is in Egypt. The contributions of these dedicated personnel will be missed. Replacements are shown in the manpower table.

FUNDING

Funding for FY84 was in line with previous funding. It promises to look generous compared to the future. In addition there was \$24,746 spent for travel to report findings at professional meetings and \$835.78 for reprints.

A small, but significant, item is computer support. WBAMC chose to have uniformity in small business computers to provide hardware and software support. Both objectives are near realization and our capabilities in DCI have expanded to meet needs that result from more support and regulatory constraints with the same personnel and less funding.

PROGRESS:

FY84 saw 41 published articles, 39 articles accepted for publication, and 14 submitted by personnel currently at WBAMC or for work done while at WBAMC. In addition, there were 84 presentations in scientific arenas. Our efforts show an increase with two possible explanations: Residency review committees are taking a more critical look at programs with attention paid to research and publication efforts. Second, WBAMC established a scientific awards committee and granted \$1250 to fifteen individuals whose research or publications were judged to have exceptional merit. There is, therefore, more external pressure to publish and more real benefit to notify the Department of Clinical Investigation of publications or presentations.

MANPOWER

<u>Title</u>	Recognized Requirement (SSI/MOS)	Auth	Assigned	Name
OFFICE OF CHIEF				
Chief	60M9B	0-6	0-6	Weir, M.R.
Alled Sci (Biochem)	68C9B	0-3	0-4	Smith, M.L.
Editorial Asst	01087	GS-7	GS-7	Casteel, P.J.
Protocol Coord	01087	-	-	-
Clerk, Supply	02005	GS-4	GS-4	Turner, L.
Internist	61F00	-	-	-
CHEMISTRY SERVICE				
Supv Res Chem	01320	GS-12	GS-12	Rauls, D.O.
Biochemist	68	-	-	-
Chemist	01320	GS-9	GS-9	-
Bio Sci Asst	01H20	E-5	E-5	Brady, Ann
Med Lab Tech	00645	GS-7	GS-7	Manna, B.S.
Med Lab Tech	00645	GS-7	GS-7	Lund, M.
Med Lab Tech	00645	-	-	-
Med Lab Aide	00645	-	-	-
MICROBIOLOGY SERVICE				
Supv Microbiol	00403	GS-12	GS-12	-
Immunologist	68 E9B	0-3	0-3	Serio, C.S.
Bio Sci Asst	01H20	E-5	E-4	Fama, Dominick
Microbiologist	00403	GS-9	GS-9	Barren, P
Med Lab Tech	00645	GS-7	GS-7	MacIntyre, S.
Med Lab Tech	00645	-	-	-
Med Lab Tech	00645	-	-	-
Electron Micr Tech	00699	-	-	-
BIOLOGICAL RESEARCH SERVICE				
C, BioRes Svc	64C9B	0-3	0-4	McNamee, G.A.
Vet Anm Sp	91T20	E-5	E-4	-
Animal Care Sp	91T20	E-5	E-4	Ramirez, C.
Vet Anm Sp	91T10	E-4	E-4	-
Vet Anm Sp	91T10	E-4	E-4	Sedivy, P.
Vet Anm Sp	91T10	E-3	E-2	Yarborough, K.
Vet Anm Sp	91T10	E-3	-	-
Hlth Tech	00699	GS-7	GS-7	Revels, J.E.
Anm Caretaker	05048	WG-1	WG-1	Burton, A.D.
Anm Caretaker	05048	WG-4	WG-4	Sigholtz, J.
Lab Animal Tech	00704	-	-	-

Replacements not shown are indicated in Personnel Section

EXPENDITURES	FY81	FY82	FY83	FY84
Personnel (Civilian)	198,298	191,190	207,914	241,950
Consumable Supplies	86,351	122,189	120,660	108,370
MEDCASE Equipment	203,884	77,965	248,000	161,166
Capital Equipment	36,256	34,144	9,643	7,263
TDY	2,387	4,743	2,767	3,772
Contracts, Services,				
Printing & Reproduction	5,905	2,982	6,242	8,874
TOTAL	531,081	433,213	595,226	531,395
Military Pay	217,503	259,726	245,853	257,631
	748,584	692,939	841,079	789,026

	Protocols Ongoing 1 Oct	New Protocols Submitted During FY	Total Protocols	Protocols Completed During FY	Protocols Terminated During FY	Publications and Presentations	OMA Supply Budget
FY77 & 77T	53 (42)*	25 (20)	78 (62)	18 (14)	15 (12)	24 (19)	\$56,831 (\$45,465)
FY78	45	30	75	3	9	28	\$35,923
FY79	63	43	106	9	14	46	\$34,392
FY80	83	41	124	25	25	63	\$60,134
FY81	74	59	133	16	17	80	\$86,351
FY82	100	58	158	42	45	88	\$122,189
FY83	71	51	122	24	19	161	\$120,660
FY84	76	76	152	30	43	178	\$108,370
FY85	79						

*Figures in parentheses represent adjustment to a base of 12 months.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/33 Status: Terminated

Title:

Study of the Size and Charge Heterogeneity of Prolactin in Human Seminal Plasma and Spermatozoa

Start Date: April 1981

Est Comp Date: Dec 1983

Principal Investigator:

Facility:

MAJ Michael L. Smith, PhD

Dept/Sec: Dept Clinical Investigation

Assoc Investigators

Key Words:

Prolactin; Seminal fluid; Spermatozoa

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:\$184(716)

Review Results

Study Objective:

Prolactin in physiological fluids exists in several forms which differ in molecular weight or molecular charge. Our objective in this study is to identify these forms of prolactin in seminal plasma and spermatozoa and to quantitate them. Identifying and quantitating these forms of prolactin may eventually lead to an understanding of their roles in semen and fertility.

Technical Approach:

Semen samples from males undergoing fertility evaluation will be collected. Those samples with high sperm counts will be saved. Three aliquots of each sample, (1) semen, (2) seminal plasma, and (3) sperm extracts, will be fractionated by Sephadex chromatography and the molecular weight distribution of prolactin will be determined by radioimmunoassay of the fractions. The charge heterogeneity will be determined by isoelectric focusing and radioimmunoassay.

Progress:

The presence of immunoreactive prolactin (iPRL) in semen was reported in 1974 [1]. Subsequent reports suggested that it had a role in the regulation of various receptors [2,3] or possibly aided the process of capacitation [4]. These roles have not been well established at present. It has also been shown that total immunoreactive semen prolactin concentrations correlate with several parameters of fertility [5] and that this immunoreactive prolactin

actually exists as several species of different molecular weights [6]. The nature of these species is not known. More careful studies need to be done to first identify the number of forms of seminal prolactin based on differences in molecular weight and molecular charge. Then the functions and sources of these various forms can be investigated. Analogous studies in serum and amniotic fluid [7,8,9] have shown that amniotic fluid contains isohormones which are not present in serum and that these forms may be produced in the female reproductive tract by decidual cells [10]. These studies are not only helping to elucidate the roles of prolactin in reproduction but are introducing the relatively new concept in endocrinology of local production of mammatropic hormones.

It is important to obtain samples with sperm densities greater than 100×10^6 sperm/ml and to use them within one hour of collection [11]. This was too difficult, so only a few sperm extracts were studied by HPLC. The incomplete work is presented here and the protocol terminated.

Materials and Methods

After varying many conditions, such as extraction buffers, order of freezing, type of sonication, number of washings, etc., the following procedure was found best for storing and extracting sperm:

1. Semen analysis by the usual method [5]
2. Centrifuge at 3000g for 20 minutes.
3. Wash 2X with 0.01MPBS/pH=7.6.
4. Add 1 ml of 0.01MNaHCO₃/pH=10.0 buffer, freeze at -70C.
5. Thaw, add 1/5 volume of glass powder, sonicate for 15 minutes at -17C, let stand 4-8 hours at 4C with occasional mixing.
6. Centrifuge 1200g for 10 minutes at 8C, remove and filter supernatant with 0.22u millipore filter, adjust pH to 7.6 with 4N HCl.
7. Inject 10-200uL onto HPLC I-250 column (Waters Assoc.) using 0.01m PBS/pH=7.6 mobile phase, 1 ml/min, detect with 280 nm light.
8. Also assay supernatant for iPRL and immunoreactive HCG [12], using Serono Labs' kits. B-HCG method cross reacts 1.36% with human LH.

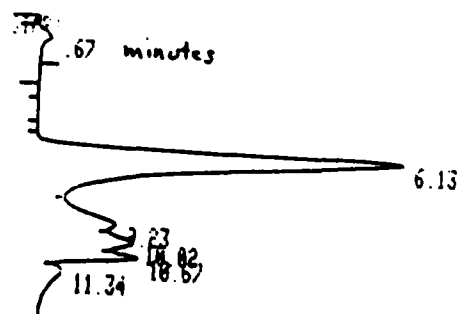
RESULTS & CONCLUSION:

TYPICAL HPLC CHROMATOGRAM

RUN # 4

AREA%	RT(minutes)	AREA	TYPE	AR/HT	AREA%
0.41	278020	D	BB	0.347	1.561
6.09	8503900	PV		0.998	47.745
9.27	1866700	VV		0.898	10.480
10.08	2737400	VV		0.848	15.369
10.70	4341200	D	VB	1.281	24.373
16.42	84028	I	BP	0.914	0.477

TOTAL AREA= 1.7811E+07
MUL FACTOR= 1.0000E+00



STOP

1. 10% of iPRL is not removed from glass powder during extraction.
2. Peak at 10.67 minutes is due to a seminal plasma protein.
3. Freezing and/or concentrating 10-fold does not change the protein chromatogram.
4. Amount of iPRL 0.05-0.3ng per 10^6 sperm
iB-HCG 1.9-2.5 mIU per 10^6 sperm.
5. Fractions from the column were not tested for iPRL or iBHCG levels.

REFERENCES

1. Sheth AR, et al: Occurrence of prolactin in human semen. Fertil Steril 26:905, 1975.
2. Keenan ET, et al: Specific binding of prolactin by the prostate gland of the rat and man. J Urol 122:43, 1979.
3. Bartke A: Role of prolactin in reproduction in male mammals. Fed Proc 39:2577, 1980.
4. Shah GV and Sheth AR: Is prolactin involved in sperm capacitation? Med Hypotheses 5:909, 1979.
5. Smith ML et al: Correlations between semen immunoreactive prolactin, sperm count, and sperm motility in prevasectomy and infertility clinic patients. Fertil Steril 32:312, 1979.
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7. Garnier PE et al: Heterogeneity of pituitary and plasma prolactin in man: Decreased affinity of "big" prolactin in a radioreceptor assay and evidence for its secretion. J Clin Endocrinol Metab 47:1273, 1978.
8. Ben-David M and Chrambach A. Preparation of bio- and immunoreactive human prolactin in milligram amounts from amniotic fluid in 50% yield. Endocrinology 101:250, 1977.
9. Ben-David M and Chrambach A. A method for isolation by gel electrofocusing of isohormones B and C of human prolactin from amniotic fluid. J Endocrinol 84:125, 1980.
10. Golander A, et al: Synthesis of prolactin by human decidua in vitro. J Endocrinol 82:263, 1979.

11. Smith ML and Lugman WA: Review: Prolactin in seminal fluid. Arch Andrology 9:105, 1982.
12. Asch RH, et al: Presence of a human-chorionic gonadotropin-like substance in human sperm. Am J Ob-Gyn 135:1041, 1979.

ACKNOWLEDGMENT:

Ms Brigetta Manna is thanked for her hard work and patience during this project.

STATUS: Terminated

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/34 Status: Terminated
Title:

Location of Prolactin, HCG, LH, AND FSH in Human Semen: An Immunocytochemical Study

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ M.L. Smith, PhD

Dept/Sec: Dept Clin Investigation Assoc Investigators
Key Words:

Prolactin; Human Chorionic Gonadotropin; Luteinizing Hormone; Follicle-Stimulating hormone; Immunocytochemistry

Accumulative MEDCASE Est Periodic
Cost OIA Cost:\$1446(1446) Review Results
Study Objective:

The hormones prolactin, HCG, LH, and FSH have been found in semen. HCG and some prolactin are known to be associated with spermatozoa. This study proposes to determine the distribution of these hormones between oval spermatozoa, other morphological cells, and seminal plasma. This will be done by immunofluorescent techniques, light microscopy, and electronmicroscopy.

Technical Approach:

Semen will be collected from volunteers. Sperm will be separated, washed, then subjected to Sternberger's peroxidase antiperoxidase reaction. They will be observed and photographed using light microscopy. If hormone binding is observed, the sperm will also be examined by electron microscopy. Hormone distribution will be determined from electron micrographs.

Progress:

Immunoreactive prolactin (iPRL) [1], LH (iLH) [2], and FSH (iFSH) [3] have been found in semen. Immunoreactive HCG (iHCG) is also present and is located primarily in the spermatozoa [4]. The roles of these hormones in male reproduction is not well understood [5]. It has been assumed that prolactin, LH and FSH are produced solely by the pituitary and enter semen via the accessory sex organs [2,6]. However, the presence of HCG in spermatozoa [4] has introduced the possibility of local production of a gonadotropic

hormone. The fact that prolactin is produced in the reproductive tract in females [7] also makes the idea of local production in males more reasonable. A detailed study of the location of hormones in semen will help to identify possible production or binding sites and may help elucidate the role of these hormones in semen. Future implications of this work will be the improvement in our understanding of infertility and endocrine diseases.

COMMENT: Personnel shortages in the Department of Clinical Investigation and Electron Microscopy Service forced us to modify the protocol. Samples were already being collected from pre- and post-vasectomy subjects after informed consent. Therefore, the plan was to assay sperm extracts and seminal plasma on these samples for iLH and iHCG. A previous study had shown that vasectomy reduced seminal plasma iLH levels by about one-half, but the method cross-reacted with B-HCG [2]. Measurements using new methods with low cross-reactivities should reveal which of these hormones was affected by vasectomy.

Materials and Methods:

Subjects scheduled for vasectomy were asked to give at least one semen sample before surgery and one after and to sign a volunteer agreement. Within one hour of collection, a portion of each sample was removed for semen analysis [6]. The remainder was centrifuged at 3000g for 20 minutes at 8C. The seminal plasma was removed and stored at -70C and the sperm pellet washed twice with 0.01MPBS/pH = 7.6. One ml of the PBS was added to the pellet and it was stored at -70C.

Seminal plasma was thawed and analyzed for iLH and iHCG. The spermatozoa were ultrasonicated for 15 minutes at -17C and the supernatant of a 1200g/10 minute centrifugation was assayed for hormones. The iLH method (American Biochemical) cross-reacted less than 3% with HCG and less than 20% with TSH. HCG was assayed with a Hybritech Kit reporting 0.24% cross-reaction with LH and less than 0.001% cross reaction with TSH.

During three years twelve subjects volunteered, seven gave samples, and only one complied with the collection criteria. The incomplete results are presented and the protocol terminated.

RESULTS AND DISCUSSION:

Seminal plasma results for six samples:

COMPONENT	MEAN	STANDARD DEVIATION	RANGE
Sperm density (X10 ⁶ cells/ml)	68.5	47.7	5.5-169
ln sperm density	3.74	1.31	
iLH (mIU/ml)	33.4	15	15-54
iBHCG (mIU/ml)	1.2	1.1	0-4

Seminal plasma iLH correlated with sperm density ($r = 0.47$), but had $p > 0.1$ for the small number of samples. All HCG values were near the limit of detection.

BHCG from the sperm extracts was less than 5.0 mIU/sample for all samples. iLH achieved a maximum concentration of 40-50 mIU/ml PBS regardless of sperm density.

It appears that HCG interferences were small in the iLH values reported earlier [2]. However, this is not conclusive since the HCG results are inconsistent with previous findings. The HCG kit from Serono Labs, 1.36% cross reaction with LH, detected significant amounts of HCG in sperm extracts, (see Protocol 81/33) and the Hybritch method did not.

Acknowledgment: Mrs Brigitta Manna is commended for her hard work and excellent recordkeeping.

REFERENCES

1. Sheth AR et al. Occurrence of prolactin in human semen. Fertil Steril 26:905, 1975.
2. Smith ML, Luqman WA: Seminal immunoreactive luteinizing hormone before and after vasectomy. Clin Chem 26:1068, 1980.
3. Biswas S et al: Fructose and hormone levels in semen: Their correlations with sperm counts and motility. Fertil Steril 30:200, 1978.
4. Asch RH et al: Presence of a human chorionic gonadotropin-like substance in human sperm. Am J Obstet Gynecol 135:1041, 1979.
5. Luqman WA, Smith ML: Hormones in semen. 1st SEAP Congress of Clinical Biochemistry. Singapore. October 1979.
6. Luqman WA, Smith ML: Seminal immunoreactive prolactin before and after vasectomy. Clin Endocrinol 10:213, 1979.
7. Golander A et al: Synthesis of prolactin by human decidua in vitro. J Endocrinol 82:262, 1979.
8. Sternberger LA et al: The unlabelled antibody enzyme method of immunohistochemistry. Preparation and properties of a soluble antigen-antibody complex (horseradish peroxidase-antihorseradish peroxidase) and its use in identification of spirochetes. J Histochem Cytochem 18:315-333, 1970.

STATUS: Terminated

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/36 Status: Ongoing

Title:

Phase II Studies on Ketoconazole (Keto) - Comparison of Two
Different Doses of Keto in Treating Coccidiomycosis

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Idelle Weismann, MC

Dept/Sec: Dept Clinical Investigation

Assoc Investigators

Key Words:

Coccidiomycosis; Ketoconazole

MAJ S. Smith, MC

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the most efficacious dose of Keto for humans with coccidioidomycosis. To evaluate the toxicity of Keto in humans with doses up to 1600 mg per day. To evaluate the CSF penetration of very high doses of Keto.

Technical Approach:

The details are lengthy and specified in the original protocol, which is on file in the Dept Clinical Investigation, WBAMC, and is available upon request.

Progress:

Annual review of this protocol was conducted in September 1984. Two patients have been entered into this study during the past year. Neither patient responded to Ketoconazole, were changed to Amphotericin B, and did well on this medication.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/59 Status: Terminated

Title:

Restriction Enzyme Analyses of E. Coli Bacterial Chromosomes and Their Membrane-Associated Sequence

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Dept Clinical Investigation

Assoc Investigators

Key Words:

DNA Membrane bound sequences

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

The objective will be to analyze membrane associated chromosomal DNA sequences to determine specificity and possible function as a regulatory mechanism in bacterial growth.

Technical Approach:

Bacterial nucleoid isolation and the determination of membrane bound DNA fragments will be done as described previously. A refined quantitation scheme incorporating an improved method for agarose gel electrophoretic analysis of restriction enzyme fragments will be used to estimate the average size of membrane associated DNA. We can then calculate the average number of inherent membrane attachment sites on the bacterial chromosome. These estimates will be compared with results obtained using different restriction enzymes and the techniques reported in the literature. Comparable numbers will add validity to the technique since these should not vary significantly from enzyme to enzyme despite very different average segment size. Isolated membrane associated DNA fragments will be analyzed to determine if they are a unique subset of the entire chromosome by performing rehybridization kinetics and second restriction enzyme analyses. If successful, pulse labeling experiments will be done using E coli mutant strains with temperature sensitive replication mechanisms. Comparative studies of specific DNA fragments can then be done by hybridization assays using labeled probe from temperate phage carrying known sequences of the bacterial DNA.

Progress:

No technical help was obtained and the principal investigator was subsequently transferred. Therefore, this project has been terminated.

Detail Summary Sheet

Date: 01 Oct 84 Prot No: 82/61 Status: Terminated
Title:

Use of Flow Cytometry to Isolate Novel Revertants of E. coli
Partition Deficient Mutants

Start Date: Est Comp Date:
Principal Investigator: Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Dept Clinical Investigation Assoc Investigators
Key Words:

Flow cytometry; Bacterial mutant enrichment

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

This study is planned to evaluate the use of flow cytometry as an enrichment process in procedures for the isolation of bacterial mutants.

Technical Approach:

Escherichia coli DNA partition (PAR) mutants will be used for the initial screening procedures. At temperatures over 40°C, these mutants stop cell division but continue to replicate their DNA resulting in enlarged cells with four to eight genome equivalents DNA. The first objective will be to establish that the mutant phenotype can be distinguished from wild type cells in the Ortho Cytofluorograph. Cultures will be given at 41°C and 30°C, diluted and mixed with media containing ethidium bromide (DNA stain). The mixed culture will be sorted on the basis of cell size and quantity of DNA (fluorescence intensity) per cell. The efficiency of sorting will be evaluated by microscopic examination under phase and fluorescence illumination. Once the separation conditions are determined revertants may be selected on the basis of their wild type phenotype when grown at 41°C. After sorting, single colony isolates will be screened for temperature sensitivity, i.e., ability to multiply at 41°C. Intragenic or suppressed revertants should grow while extragenic or second site revertants may or may not. Those that did not have the PAR phenotype, but could not grow at 41°C would be the strains of interest initially. Such novel revertants would establish the feasibility (the technique and possibly lead to further insight on the problem of the regulation of bacterial growth.

Progress:

Principal investigator was transferred and the study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/62 Status: Ongoing

Title:

Analyses of Copper Complexes in Plasma

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

David Rauls, PhD, DAC

Dept/Sec: Dept Clinical Investigation

Assoc Investigators

Key Words:

Copper salicylates

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To develop methodology for the analysis of copper salicylate complexes in plasma and measure blood levels attained upon administration of these complexes to rats.

Technical Approach:

Copper diisopropyl salicylate will be prepared by literature methods. Optimum conditions for analysis of the complex by high performance liquid chromatography will be worked out on the pure substance followed by isolation of the complex from spiked plasma to determine recovery and interferences. Attempts will be made to utilize atomic absorption spectroscopy for quantification of the complex in order to obtain adequate sensitivity. Once the accuracy, precision, and sensitivity of the assay have been established, the copper diisopropyl salicylate will be injected into rats intraperitoneally at doses (100 mg/kg) found to inhibit maximal electroshock seizures in rats. Blood samples will be analyzed at 0.5, 2, and 4 hours post-injection. The existence of the intact copper complex in plasma will be considered proven if a copper containing peak is recovered from injected rat plasma having a HPLC retention time equivalent to that of the pure copper diisopropyl salicylate and such a peak is found to be absent from a plasma sample from a rat injected with vehicle only.

Progress:

Copper diisopropyl salicylate has been prepared and characterized. No further work has been accomplished during the past year because of time constraints. Work will continue on this project.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/14 Status: Ongoing
Title:

Immunomodulating Effects of Terbutaline in Humans

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT C.S. Serio, MSC

Dept/Sec: Dept Clinical Investigation Assoc Investigators
Key Words:

Terbutaline

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To provide experimental evidence that the beta-adrenergic agonist terbutaline may have an effect on cells involved in various immunological processes such as cell mediated and humoral immunity.

Technical Approach:

Forty healthy nonpregnant volunteers will be selected at random from staff and technicians from the various departments of the hospital. The physicians in charge will thoroughly explain the implications of this study and the use/contraindications of terbutaline injections. The volunteers will be divided into four groups of 10 each. All volunteers will have three 10cc tubes of blood drawn on Day 0 for control samples. Group A controls will receive 0.5cc subcutaneous injections of saline (i.e. saline controls). Groups B, C, and D will receive total doses of 250, 500 and 750ug terbutaline sulfate subcutaneously. At days 4, 7, 9 and 14 post-terbutaline or saline injection blood samples will be taken and examined.

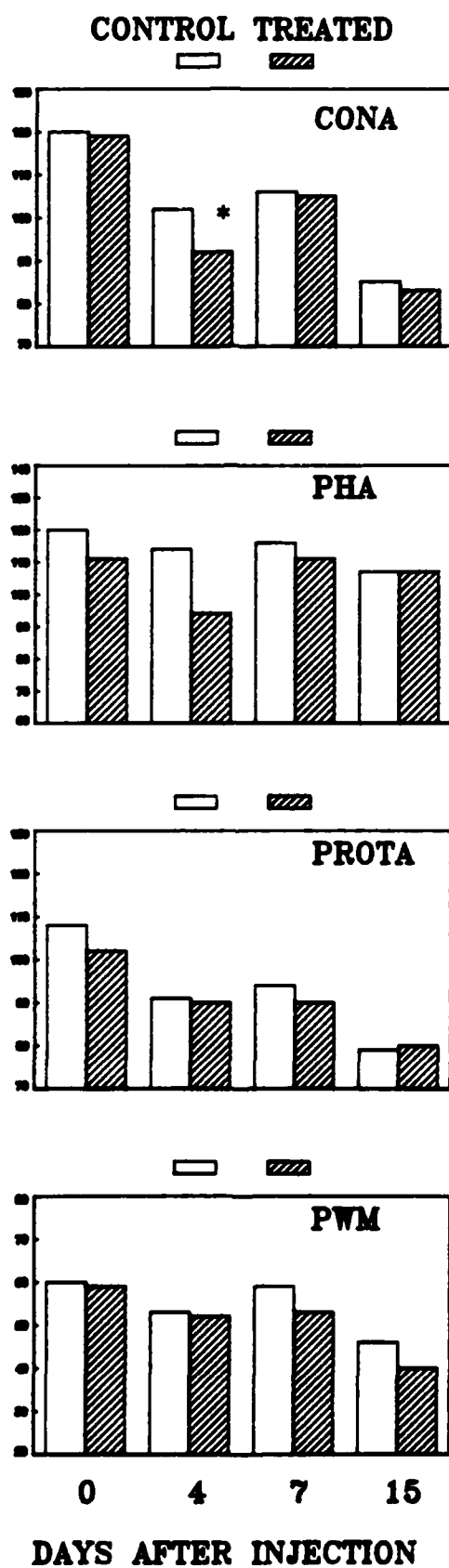
Progress:

The results of a single subcutaneous injection of 7.0ug/kg of terbutaline sulfate in 40 human volunteers are presented in Fig 1. The dose per subject ranged from 350ug to 650ug. Four days after the single injection the group receiving terbutaline sulfate demonstrated a suppressed CON A-induced lymphoblastogenesis when compared to saline-injected control subjects. The lymphocyte responsiveness using other mitogenic stimulants (PHA, Protein A and PWM) between terbutaline injected and control individuals were not significantly different.

In the second experiment which investigated terbutaline dose effects, the high and low dose (Group 5) had mean lymphocyte response values on Day 4 of 109 ± 7 and $96 \pm 6 \times 10^3$ CPM/ 2×10^5 cells, respectively, compared to $120 \pm 13 \times 10^3 / 2 \times 10^5$ cells for the saline control group. Although suppression was apparent, it was not statistically significant due to the small number of subjects per group. Lymphocyte suppression was not observed on Days 7, 9, and 14, and there was no statistical differences between any group values on any day when PHA or protein A were used as mitogens.

The mechanism through which terbutaline sulfate produces suppression in the human lymphocyte in the presence of CON A remains unknown. Since normal values were observed with all other mitogens tested, the data suggest that the suppression noted was possibly mediated through subsets of T-lymphocyte responsive only to CON A. We are presently continuing our investigation into the observed suppression in an attempt to elucidate the mechanism(s) as to receptor site changes, T-cell subset involvement, and role of terbutaline on the lymphoid tissues.

LYMPHOCYTE RESPONSE X 10^3 PER 2×10^5 CELLS



*P < 0.05

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/21 Status: Ongoing

Title:

Development of a Simple, Rapid and Reproducible Chemotaxis Assay for Clinical Use

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT C.S. Serio

Dept/Sec: Dept Clin Investigation

Assoc Investigators

Key Words:

Chemotaxis assay

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To provide the clinical laboratory with a chemotaxis assay to measure defects in neutrophil and macrophage function in disease states such as recurrent bacterial infections and tumor insult.

TECHNICAL APPROACH:

Our plan is to develop the methodology and hardware for a chemotaxis assay which will allow for the following:

1. A simple assay that will allow a technician to perform the test with little or no training.
2. A reproducible slide technique in which the quantitation of cell movement can either be made by a scanning spectrophotometer or densitometer (instruments that are inexpensive and common in most laboratories). In addition, the slides are inexpensive and may be stored as a permanent record or discarded.
3. A slide prepared with the positive and negative chemotactic agents that can be stored in a freezer and utilized immediately upon thawing.

Experimental Design

We will utilize a lab-tek culture dish as an incubation chamber for both the chemotaxin and the cells to be tested. This chamber consists of eight separate plastic wells (volume .5 ml per well) separated by a nontoxic rubber gasket mounted on a microscope slide. The chemotaxic agent(s) will be combined with agarose (0.4% in Hanks balanced salt solution) and placed in each of the four top test chambers at approximately 39°C and allowed to solidify.

The positive chemotaxins to be utilized in this study will be N-formylmethionyl-leucyl-phenylalanine-methylester and human serum derived complement component C5a (These factors once embedded in the agarose will be frozen at -20° for their freezer life and tested). Negative controls will be normal saline in agarose.

Initial studies will be performed with freshly prepared chemotaxins. After the agarose has solidified approximately 2×10^5 test cells will be placed in opposite wells from the chemotactic factors and the slide placed at a 45° angle for 30 minutes at 37°C to allow for the attachment of neutrophils on the side of the chamber closest to agarose. By doing this, we virtually are lining up the cells on an imaginary starting line. After the initial 30 min incubation, the top plastic wells will be removed off leaving the base rubber gasket in place to act as a border between cells and agarose. The rubber gasket between each set of test wells will then be cut with a scalpel and 100 ul of media (Hanks balanced salt solution) added to the cellular side to allow contact with the agarose embedded chemotactic factor. This contact between media and agarose will result in a gradient formation and the subsequent dispersal of chemotaxins out of the agarose toward the cells. A plastic cover will be placed over the rubber gasket at this time and the slide reincubated in a 5% CO_2 incubator at 37°C with 95% humidity. After an incubation period of 2-3 hours, the rubber gasket will be removed, the slides washed in saline, fixed in methanol and stained. The slide will then be mounted on a scanning stage of a Gilford Spectrophotometer and scanned for optical density for the number of cells that have actually migrated toward the chemotactic factor. Preliminary standards for various cell numbers on each slide will be established at different spectrophotometer settings and various slit widths in order to establish maximum sensitivity. Background readings will be taken with standard microscope slides.

Progress:

No progress due to personnel losses.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/37 Status: Ongoing

Title:

Cardiopulmonary Effects of Stressful Exercise at 4,000 feet on SCT Individuals

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ I. Weisman, MC

Dept/Sec: Dept Medicine/Pulmonary Cl

Assoc Investigators

Key Words:

Sickle cell trait; stress

Accumulative MEDCASE

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OMA Cost:

Review Results

Study Objective:

a. To establish baseline pulmonary function data (spirometry, helium dilution lung volumes, Maximum voluntary ventilation L/min (MVV), Arterial blood gas analysis (ABG), single breath diffusing capacity D_LCO_{SB} (ml/min/mmHg) and steady state diffusing capacity D_LCO_{SS} (ml/min/mmHg) (Filley technique) as well as values for the partial pressure of oxygen at 50 saturation (mmHg) (P_{50}) in Hgb AS individuals and controls and to determine percent Hgb S and percent Hgb F in individuals heterozygous for sickle cell trait (Hgb AS) at 4000 ft.

b. To carefully document cardiopulmonary response of individuals identified as having Hemoglobin AS during both strenuous incremental and submaximal steady-state exercise at altitude with age, race, sex, smoking, matched non-Hgb AS controls.

c. To correlate observed abnormalities (if any) in parameters of cardiopulmonary performance with levels of Hgb S in individuals with sickle cell trait (i.e. are patients with 40 percent of Hgb S more likely than controls to experience abnormalities during vigorous exercise. Also, to determine whether Hgb F levels may be protective as they are in patients with sickle cell disease.

d. To determine whether conditioning (repeat studies after six weeks) is operative in modulating cardiopulmonary performance in both SCT individuals and controls.

e. Conclusive data is not anticipated from this protocol, but a preliminary statement or suggestion may be offered on the important question of occupational restriction of subjects with Hgb AS. This is in keeping with the National Academy of Science - National Research Council's Report of 1973 [1].

Technical Approach:

Phase I (Initial Screening): Approximately 30-35 heterozygous sickle hemoglobin individuals (AS) and a similar number of age, race, smoking, physically conditioned matched normal volunteers (AA) to be used as controls will be studied. Hopefully, the numbers of participants will be screened from incoming recruits at Ft Bliss (four Hgb AS subjects - four normal controls/month). An initial positive screening blood test (modified Sickledex) will be followed up by hemoglobin electrophoresis and Hgb S and Hgb F quantification in order to exclude the possibility of actual SS disease itself and sickling variants other than hemoglobin AS (i.e., Hgb SC, sickle thalassemia, etc). Previous studies have failed to fully characterize the nature and quantity of Hgb S present in patient populations.

Once identified, the Hgb AS individuals as well as subjects to be used as normal controls will be asked to participate in the study acknowledging by signed informed consent.

Phase II. Prior to the initiation of exercise the following will be performed on the Hgb AS and control subjects. a) History and physical exam with chest x-ray. b) Blood work - baseline CBC, peripheral smear (best method to be determined in order to quantify and compare with samples taken during exercise), G-6-PD screens, SMA-20 including CPK and aldolase, and serum osmolality. c) Urine-baseline, urinalysis and urine osmolality, checking specifically for concentrating defects, RBCs in urine, etc. d) Baseline pulmonary function tests to include (1) spirometry (2) MVV (3) helium dilution lung volumes (4) D_LCO_{SB} (1-4 to be performed on pre-existing Collins-DS-520) (5) a resting ABG, 100 O_2 ABG study (to determine percent $R\ddot{o}$ L shunt) (6) P_{50} value (7) 2,3 DPG level. (8) baseline 12-lead EKG - individuals with abnormal baseline EKG (to be determined by staff cardiologist) and Hgb AS individuals with abnormal EKGs will not be included in this study. They will be referred to Cardiology for appropriate evaluation which may include being exercised in the cardiac cath lab (questionable data to be included in this study).

Individuals with EKGs interpreted as either sinus bradycardia and/or "early repolarization" phenomenon will be exercise-studied according to this protocol.

Individuals with abnormal baseline PFTS and normal EKGs will be exercise-studied.

Phase III. Exercise protocol - preliminary.

a. Preliminary. 1) Informed consent will be obtained from all participants. Both the M.D. and the exercise technician will be blinded as to whether the eight patients being studied monthly (4/4

are AA or AS respectively).2) Individuals will have an indwelling arterial (either radial or brachial) cannula placed with a three-way stopcock and slow or intermittent heparin infusion at a concentration of 1000 u/100 ml diluent. An arterial line will allow for measurement of PaO_2 , PaCO_2 , SaO_2 , pH, HCO_3 as well as allowing for additional blood sampling (i.e. lactate levels) during exercise. 3) A two-lead EKG signal integrated into the exercise system will be used with continuous oscilloscope display screen as well as trip recorders in the event an abnormality is noted on the screen during exercise (A physio-control lifepak with a Hewlett-Packard recorder). 4) An ear oximeter will be placed on the ear lobe and held in place with head straps allowing for the monitoring of SaO_2 and trending phenomena in SaO_2 appreciated during exercise. 5) Several preliminary exercise studies have been performed on patients with hemoglobin AS who were referred because of exercise induced problems in the last five-six months. These patients were studied using the pre-existing automated exercise system in the pulmonary laboratory. This automated system is the SRL Model 7000 Aerobic Measurement System with Model 7500 Treadmill System. This system incorporates a mixing chamber for expired gas analyses. As a result the readout from the nonprogrammable computer records only the last 20-30 seconds of data from each minute. It is important to note that the workout characteristics of mixing chambers may give erroneous results if mixed expired gas concentrations are rapidly changing (i.e. especially with rapidly incremental work rates which will be used in this protocol). An exercise system which allows for breath by breath analysis allows one to follow the changes of rapidly incremental exercise more accurately than a mixing chamber and would be preferable for our purposes. The Medical Graphics Corporation (MGC) System 2000B Cardiopulmonary exercise module would satisfy the requirements of this protocol design. A $\text{D}_L\text{CO}_{\text{SS}}$ (MGC) apparatus can be interfaced with the breath by breath exercise system without difficulty. With our present system it is not possible to retrieve data not initially requested because there is no memory bank in the present computer. The computer is nonprogrammable and the data profile is that which accompanies the system and not necessarily what the investigator needs.

A treadmill for the purpose of pulmonary exercise, especially with healthy, otherwise normal individuals, appears to be suboptimal compared to a bicycle ergometer where the position of the head is more stationary allowing for better control of the ear oximeter and the mouthpiece. 6) The patient will be allowed to familiarize himself with the equipment - treadmill or cycle ergometer and especially breathing through a low resistance, low dead space mouthpiece (Keogh or Lloyd). Exercise will be performed with a technician trained in CPR as well as an M.D. present.

Exercise protocol:

The exercise protocol is a one-minute incremental exercise test to exhaustion over a 6' - 10' interval [16]. When stable baseline measurements of minute ventilation, heart rate, mixed expired PO_2 and PCO_2 are established, exercise begins. The individual exercises at workloads increasing by 150 kpm (equivalent 25 watts) at one minute intervals. Minute by minute readout of the following parameters will be evaluated: Mixed expired PO_2 and PCO_2 , tidal volume (T.V.), respiratory rate (RR), minute ventilation (V_E), VO_2 (oxygen consumption), V_{CO_2} (CO_2 consumption) RQ = respiratory quotient (V_{CO_2}/VO_2), heart rate.

(H.R.), V_D/V_T , (dead-space ventilation). At or near anaerobic threshold, ABGs and a lactate level are drawn from the arterial line. When the patient signals exhaustion another sample will be obtained and the test will be discontinued. Factor VIII levels will also be drawn. The highest Minute ventilation (V_E) (Respiratory rate X tidal volume) oxygen consumption VO_2 (L/min) and heart rate (H.R.) recorded will be considered the maximal V_E , max VO_2 and max H.R. With rapid incremental exercise the individual will recover quickly and can be restudied in 30-45 minutes.

Recovery ABGs as well as above parameters will be obtained at that time.

b. After approximately 30-45' from completion of the rapidly incremental exercise test, the individual will perform a resting D_LCO_{SS} maneuver (Filly modification of steady state technique) to be used as baseline. Subsequently the individual will work at a steady state submaximal level (≈ 50 of VO_2 -max established by incremental study) capacity for another 6' during which an exercise D_LCO_{SS} will be performed. A repeat ABG in order to obtain $PaCO_2$ and enable V_D/V_T determination will be obtained. Minute by minute printout of the $PeCO_2$, $PeCO$, $PACO$ will be obtained with particular attention to the data generated during the last 1/2 to 1 minute of the steady state exercise. From the above measurements minute by minute D_LCO_{SS} will be computed [18].

c. Repeat incremental exercise test and D_LCO_{SS} at rest and with submaximal exercise after 6 weeks of basic training. This aspect of the study is important in terms of establishing whether conditioning may be operative in attenuating the differences if any in the exercise performance of the two groups. In addition, considerable data will be generated in the control population which will enable objective determination of conditioning responses which may be of assistance to the Department of the Army.

Phase IV. Evaluation of data:

a. Consent forms and all other data generated from WBAMC will be maintained along with exercise study reports in the Pulmonary Service of WBAMC. Copies of this data will be available to appropriate individuals through command channels.

b. Evaluation of data: 1) Results of baseline spirometry, MVV, Helium dilution lung volumes and single breath diffusing capacity will be expressed as a percent of published predicted values. Standard descriptive statistical analysis, involving paired Student t-test and analysis of variance will be performed within and between group differences. The data, especially that generated in the control population, may help serve to establish new predicted values for $D_{LCO_{SB}}$ and spirometry in black individuals. This is badly needed since those presently available are suboptimal [19]. Dr. Ben Burrows has agreed to serve as consultant for this aspect of the project. 2) Exercise - Criteria established by Jones et al. [16], and Wasserman et al [17] will provide predicted values for indices of exercise performance measured during the study. Gas exchange data during rest and exercise ($PaCO_2$, PaO_2 , (A-a) PO_2 , $D_{LCO_{SB}}$ ml/min/mmHg, V_E l/min, VD/VT , VCO_2 (L/min), VO_2 (l/min) and RQ .) in both the Hgb AS subjects and controls will be analyzed using both Student paired t-test and analysis of variance in order to establish differences between rest and exercise and between the two groups.

Next the Hgb AS group will be categorized according to absolute levels of Hgb S. Correlation of individual parameters with levels of Hgb S will be performed by standard regression analysis in order to determine if the levels can be predictive of abnormal cardiopulmonary response. The exercise physiology laboratory, UCLA, Harborview Medical Center, will serve in a consultant capacity for exercise related questions during the study.

Progress:

Twenty-five SCT study patients and 16 controls have undergone acute exercise testing. Four abstracts have been submitted. The next phase of the study will involve endurance testing.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/50 Status: Ongoing

Title:
Effects of Terbutaline on Lymphocyte Receptors

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ M.J. Smith, MSC

Dept/Sec: Dept Clin Investigation Assoc Investigators

Key Words:

B-adrenergic receptors; lymphocytes

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

OBJECTIVE: To determine the effect of a single dose of terbutaline on beta-adrenergic and concanavalin A (con A) receptors in mouse and human lymphocytes.

Technical Approach:

The project will be approached by (a) developing the needed assays, (b) conducting animal trials, and (c) conducting human trials.

a. Assays

(1) A beta receptor assay developed by Dr. Burman at WRAMC will be established in our laboratory. In brief, the assay is a Scatchard analysis of lymphocyte beta receptors using ¹²⁵Iodocyanopindolol. It requires lymphocytes from 16 ml of blood for humans or the spleenocytes from one mouse. The receptors will be measured on the day of sample collection.

(2) Cyclic AMP-RIA kit (New England Nuclear) analysis of lymphocyte cytoplasm will be used.

(3) Cyclic GMP-RIA kit (New England Nuclear) analysis of lymphocyte cytoplasm will also be used. The cyclic AMP (cAMP) and GMP (cGMP) measurements will be important since changes in their concentrations indicate the level of receptor activity prior to collection of the lymphocytes. Samples for analysis will be stored at -20C and run in batch for both cAMP and cGMP.

(4) A concanavalin A (conA) receptor assay will be developed using a fluorescent activated cell sorter. In brief, Carbazol dye [6] will be bound to the lymphocytes and the receptor number determined by laser analysis of each sample. Binding affinities of the receptors will be determined by quantitation of bound and free conA using Scatchard analysis. The receptors will be measured on the same day as sample collection.

b. Mouse Study.

Two groups of inbred male mice, 60 mice per group, will be injected ip. Group I, control group, will receive saline. Group II, experimental group, will receive 250 ug/kg of terbutaline sulfate in saline. Twelve mice per group will be anesthetized in the morning at days zero, two, four, seven and fourteen after injection, using Ketamine/xlazine and their spleens removed. They will then be killed by cervical dislocation, and their spleenocytes harvested by established techniques [7]. Spleenocytes from six of the twelve mice will be processed and beta receptor density and binding constants determined [5]. Cyclic AMP and cyclic GMP will be measured in the supernatant of the processed lymphocytes [8].

ConA receptor concentrations and binding constants will be determined for spleenocytes from the other six mice killed on the day of interest using techniques developed in Part A (4).

Lymphocyte transformation using conA [9] will be determined on a portion of the lymphocytes from the twelve mice killed on the day of interest.

c. Human Study.

Two groups of adult male humans, ages 20-49 years, twenty control and twenty experimental, will be studied. They will receive a single subcutaneous injection of 0.2 cc of saline or 250 ug of terbutaline sulfate in 0.2 cc of saline, respectively. In the morning of days zero, two, four, seven, and fourteen, after injection, thirty cc of peripheral blood will be taken and the lymphocytes separated as previously described [9]. These lymphocytes will be divided for beta receptor, cAMP, cGMP, conA receptor, and lymphocyte transformation assays.

d. Statistics

GROUPS

Group I - saline control

Group II - terbutaline treated

VARIABLES OR PARAMETERS

Beta receptor density (number/lymphocyte)
Beta receptor binding strength
Con A receptor density (number/lymphocyte)
Con A receptor binding strength
Lymphocyte transformation (counts/min of incorporated
³H-thymidine)
cAMP/cGMP concentration ratio.

TIME

Variables measured at 0, 2, 4, 7, 14 days post-injection.

QUESTIONS

- Q. 1. Is the control group different from the experimental group for any mean variable value on a given day?
Q.2. Is the control group different from the experimental group for all variable or subsets of the variable?
Q. 3. Which variables are associated?
Q. 4. Is the response of each variable with time different for the control and experimental group?

METHODS

Question one will be answered using a Student's t-test with paired values. Question two will be answered using a multivariate analysis of variance and covariance. Question three will be answered by regression analysis. Question four will be answered using a multivariate analysis with time.

Progress:

A single intraperitoneal injection of either 0.5 or 1 mg/kg of terbutaline sulfate significantly reduced Con A stimulated mouse lymphocyte response even four days after injection. The ability of the lymphocytes to produce antibodies was also significantly reduced. An abstract and a manuscript are listed below. Receptor assays have not been developed due to personnel shortages.

Smith ML, Mansfield LE, McIntyre SK, Serio CS: Effects of a Single Injection of b-Adrenergic Agent on Murine Lymphocyte Response. American College of Allergists Annual Meeting, San Francisco, CA, Apr 84. Manuscript has been submitted.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/03 Status: Terminated
Title:

Evaluation of Commercial Extracts Used for Allergy Diagnosis and treatment

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Assoc Investigators
Robert J. Frederick, PhD

Key Words:

Allergy

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To establish if commercial allergen extracts contain all the relevant antigenic problems recognized by allergic human beings.

Technical Approach:

Allergen immunotherapy is an effective means of treating allergen disease. This has been proven in double blind studies. However, for reasons which remain unclear in many cases, the beneficial effects are less than optimal and in some cases nonproductive.

Allergy diagnosis is by clinical history, various physical criteria, and by methodology to detect reagenic antibodies. The most important antibodies appear to be of the IgE class of immunoglobulins, although other classes of immunoglobulins are likely involved. All present methodologies used to measure IgE specific antibodies are based on commercial extracts whether they are in vitro or in vivo.

It has been shown that under usual storage conditions some of the total allergenic activity of these commercial extracts occur. Similarly it has been shown that freshly obtained commercial extracts of these same allergen vary from company to company, and within the company's product itself.

It is likely that this has an adverse effect on allergy diagnosis and treatment.

Until recently, except with extrusive biochemical separation, it has been difficult to approach allergens as simple single proteins. Instead, most of our information concerning their relevance and importance has been based on studies of mixtures of proteins, some of which are not allergens.

At William Beaumont we have developed an enzyme based overlay technique which makes it possible to look at the individual proteins contained in a mixture and defined by human serum antibodies.

For the present study, we wish to explore the possibility that commercially prepared extracts are deficient in proteins which are present in fresh pollen to which the allergic patient is exposed.

Progress:

Terminated. Principal investigator has resigned from the Army.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/07 Status: Ongoing
Title:

Effect of Levamisole and Vitamin A as Immunopotentiators Against
Lewis Lung Carcinoma.

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT Charles S. Serio, PhD

Dept/Sec: Dept Clinical Investigation-~~Assoc~~ Investigators
LTC Lyndon E. Mansfield, M.D.

Key Words:
Levamisole
Lewis Lung Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To monitor the therapeutic effects of a levamisole and vitamin A in
the growth patterns of Lewis lung carcinoma cells in C57 black mice.

Technical Approach:

Animals: C57 BL/6 female mice 6-8 weeks old (15-20g) will be
utilized in these experiments. The animals will be obtained from
Jackson Laboratory, Bar Harbor, Maine.

Tumor: Lewis lung carcinoma currently maintained in both
syngeneic mice and in vitro in our laboratory will be utilized as
the tumor model. This tumor was selected because it is widely used
by NCI in screening for potential antineoplastic agents.

Drugs: Levamisole and vitamin A will be aliquoted from single
samples. Dose levels and administration of levamisole will be based
on the reports of Renoux and Renoux [4]. These doses will be
expanded to cover a 100-fold dose range below toxic levels. Doses
and administration of vitamin A will be in accordance with
previously published methods [6]. Drug solutions will be prepared
immediately prior to administration when a single injection
treatment schedule is employed. For multiple-treatment and
combination treatment, drug solutions will be prepared at the
beginning of treatment and stored at 4°C in amber bottles.

Methods

Tumor growth determination: The growth of subcutaneously inoculated Lewis lung carcinoma (10^5) will be determined directly by excising and weighing the primary tumor or indirectly by taking caliper measurements of perpendicular diameters and estimating the tumor mass by the formula [7].

$$\text{mass(in mg)} = \frac{\text{major diameter (in mm)} \times \text{minor diameter}^2(\text{in mm})}{2}$$

The number of macroscopic lung metastases will be determined by the india ink insufflation technique of Wexler [8].

Injection schedule and data to be collected will be performed according to the outlines in Table 1 and 2.

Progress:

One hundred and fifty C51BL mice have been treated to date with both Levamisole and Vitamin A alone, in various combinations pre- and post-tumor (Lewis Lung Carcinoma) injection. Preliminary data indicates that the pre-treatment group developed about 50% less metastatic lung tumors than those animals injected at various times post-tumor injection. It appears that both high and low dose Levamisole (5 AV 0.5mg/kg) groups were not significantly different in the number of metastatic lung lesions observed. Those groups pretreated with Vitamin A alone were not significantly different from control nontreated normals which were 50% higher than the Levamisole and Levamisole/Vitamin A groups in numbers of metastatic lesions observed. None of the Levamisole or Levamisole Vitamin A groups treated post-tumor were significantly different from control values. This preliminary data allows us to narrow the treatment regimens that appear to be beneficial. We are currently continuing this investigation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/21 Status: Ongoing
Title:

Assessment of Immunological Potential of Ivermectin, A Potent New Antiparasitic Agent.

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT Charles S. Serio, PhD

Dept/Sec: Assoc Investigators
MAJ S. Ting, MC

Key Words:
Antiparasitic agent

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To assess the role of Ivermectin as a possible new immunomodulator.

Technical Approach:

a. Animals: C57BL mice will be utilized as the animal model.

b. Dosage and Injecting Schedule: Dose levels and administration of ivermectin will be based on a previously published findings [1]. In preliminary experiments, we will examine a wide range of doses (all below toxic levels) and measure various immune functions at various times after injection to establish these time and dose kinetics for either stimulation or inhibition by lymphocyte stimulation and quantitative antibody production assays.

c. Immunological measurements.

1. Lymphocyte stimulation. These assays will be utilized as an in vitro correlate of cell mediated immunity, mouse splenic, lymph node and thymic lymphocytes will be collected, separated and purified at various days after ivermectin injection (IP). T-cell responses will be analyzed by specific T-cell mitogens such as phytohemagglutinin and concanavalin A. B-cell responses will be analyzed by poke weed stimulation.

2. Antibody production. The effects of injected ivermectin on antibody production will be analyzed by using a modified plaque assay in which sheep red blood cells (SRBC) and ivermectin will be administered interperitoneally at various times before harvesting splenic lymphocytes. Control animals will receive only SRBC.

STATISTICAL ANALYSIS OF THE DATA: Statistical analysis will be performed by comparing controls (non-ivermectin injected) with experimental groups using the Student's t-test.

Progress:

Preliminary results of ongoing experiments are presented below:

I. Lymphocyte Stimulation: Results to date of the modulation by Poke Weed Mitogen (PWM) on splenic lymphocytes in C57BL mice indicates a substantial suppression in animals injected with Ivermectin compared to saline controls. This suppression to PWM stimulation was observed at both 4 days and 7 days with all injectable doses (1, 10, and 100ug). The response of lymphocytes to PHA and CON A in the saline and Ivermectin injected animals was not significantly different. However, the CON A response of lymphocytes in both control and Ivermectin animals was significantly suppressed if Ivermectin, at all doses, was added in vitro to these cells. The difference in suppression between control and injected animals was not significant in any of the additional in vitro experiments.

II. Antibody Production: Splenic lymphocytes were assayed for the production of antiSRBC antibodies in both the saline and Ivermectin injected animals. The time kinetics of Ivermectin injections (i.e. 24 hrs. pre, same time, or 24 hrs post injection) did not alter the suppressive response observed in Ivermectin injected animals compared to animals injected with SRBCs alone. The suppressive effect was dose-dependent with the lowest dose (i.e. 1 ug) being more suppressive than the higher dose tested.

Ivermectin, a potent and new antihelmintic agent, seems to modulate a number of immunological responses. The data presented demonstrates that Ivermectin can suppress PWM stimulation when given in vivo and CON A stimulation when added to tissue culture. In addition, Ivermectin, when administered in combination with SRBC is capable of suppressing antibody formation to SRBC. This study suggests that Ivermectin can act as an immunomodulator. The significance of this observed suppression and the exact lymphocyte population affected has yet to be determined.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/42 Status: Terminated
Title:

The Effects of Zaditen on the Late Phase Cutaneous Reaction: A Pilot Study

Start Date: Est Comp Date:
Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Allergy/Immunology Assoc Investigators
MAJ S. Ting, MC
R.W. Haverly, DAC

Key Words:

Zaditen

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine if Zaditen has an inhibitory effect on the late phase cutaneous reaction to allergen.

Technical Approach:

Since it has not been established that Zaditen influences the late cutaneous response, and since numerous studies have shown placebo therapy does not affect the response, this will be an open study. Ten adult nonpregnant allergic volunteers will have a late cutaneous response induced by intradermal injection of reconstituted freeze-dried allergen. The response will be performed alternately on the right forearm or on the left forearm of the volunteers. The 15 minute immediate response and the six hour response will be measured.

After this testing the volunteer will take Zaditen 2 mg BID for two weeks and then have the testing repeated with the same dose of reconstituted freeze-dried allergen which initiated the original immediate and late phase response. This testing will be done on the alternate forearm from that used at baseline testing. Measurements will be of the immediate response and the late response at six hours.

The mean lesion size at each testing time will be compared by t-testing of the difference between means.

This study will be performed under Sandoz Company IND Number 13,303 and appropriate forms provided for the FDA. The material, which has no commercial value, will be provided by the company.

Progress:

Principal investigator has resigned. No progress was reported. Study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/50 Status: Ongoing
Title:

Investigation of Methylscopolamine and Methylatropine Nitrates and Bromides Stabilities

Start Date: Est Comp Date:
Principal Investigator: Facility:

Howard C. VanWoert, Jr. PhD (Change PI to D. O. Rauls, PhD)

Dept/Sec: Dept Clin Invest Assoc Investigators
Key Words:

Methylscopolamine; Methylatropine

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine optimum, practical storage and use conditions of methylscopolamine and methylatropine nitrates and bromides.

Technical Approach:

Phosphate buffered saline solutions at pH 7.4 of methylscopolamine and methylatropine nitrates and bromides will be kept both at cold and room temperatures. Sampling of solutions will be carried out for a time span of several months. The drug potency will be evaluated every two weeks by HPLC. Each set of samples will be compared to a known set of freshly prepared standards.

Decomposition products will be identified. Assessment of these products' toxicity and effect on potency of drug will be investigated and statistical conclusions made on the basis of 90% standard deviation confidence limits.

Progress:

Newly activated protocol which is in progress. No results have been reported to date. The original principal investigator resigned and the protocol has been assumed by D.O. Rauls, PhD.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/78 Status: Completed
Title:

Career Development of Medical Service Corps Research Officers with
AMEDD

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT C.S. Serio, MSC

Dept/Sec: Dept Clin Invest Assoc Investigators
Key Words:

Career Development

MAJ M.L. Smith, MSC
LTC T.B. Jeffrey, MSC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

The purpose of this project is to survey common concerns and investigate solutions to problems of career MSC research officers. The main thrust will be to assess the feelings of these officers as to career progression, position availability, and competition for promotion.

Technical Approach:

MSC officers will be sent a questionnaire requesting that they submit suggestions and comments to establish priorities of their career development within the AMEDD. Hopefully this information will benefit present members as well as future researchers contemplating a military career, and will provide guidelines to those who are career managers of research officers. The data collected will be assimilated to represent the thinking and philosophy of research members of the R&D Command, Departments of Clinical Investigation, and clinical services. A copy of the findings will be furnished the MSC Chief, with the combined suggestions of all responding members.

Progress:

A survey was conducted of 474 junior and senior Medical Service Corps (MSC) officers within the 68 series military occupation specialties (MOS). The purpose of this survey was to assess the opinions of these officers concerning the performance of medical research in the Army and its implications toward military career development. The study population consisted of officers assigned to clinical services, Departments of Clinical Investigation, and the Medical Research and Development Command. The survey response rate was 74%. The preliminary results of a randomized sampling of twenty individuals in each rank are listed in Tables 1 and 2 and summarized below.

MSC research officers contemplating a military career will spend approximately 37% of their time on administrative duties, 25% on research, 12% on laboratory management, and 6% each on patient care, consulting, teaching, and non-MOS functions. They will publish 14 research papers in refereed journals within the 7-8 years in which they actually conduct research.

When considering promotion criteria, 80% of the 05s and below did not feel competitive with nonresearch MOS officers. Sixty-five percent of this group felt that the promotion system was unfair and that separate promotion criteria were needed. Twenty-five percent of the 06s suggested a need for a separate MSC Research Corps, compared to 50% each of the 04s and 05s, and 89% of the 03s. The effects of changing assignments while conducting research were stated to be detrimental to productivity by over 70% of those surveyed, while minimal effects and enhanced productivity were suggested by 25% of all ranks. Most 05s and below were dissatisfied with the requirement to complete advanced military education to remain competitive for promotion.

Junior officers accepted professional responsibility at a younger age and had a greater degree of control over their research projects when compared with academia. If one measures research productivity based on publications, then military researchers fell below their civilian counterparts over the duration of their career. This results from an earlier transition from a research to an administrative role, not a lack of productivity.

The years required to develop the research expertise almost equaled the amount of time performing these research duties within the AMEDD. Thus, the military is losing a valuable talent by moving these highly trained individuals into positions that could be managed by administrative officers in certain areas and are also losing valuable research productivity by reassigning officers before research projects can be completed. The average research tour was four years. Considering a conservative six-month transition time at the beginning and end of ones tour, a 20% reduction in actual research time was noted.

The process of conducting research was not a positive factor in providing opportunity for advancement/promotion for the 03-05. MSC research officers are professionals, yet their opinions suggest that they are penalized for performing the very task for which they have been employed by the military. In addition, there is a general lack of recognition for research quality.

The creation of self-worthiness and the sense of controlling career progression are essential to maintaining productivity in any organization, be it military or civilian (Peters TJ, Waterman RH. In Search of Excellence, Warner Books, NY, pp 235-278, 1984) The awareness that an individual's best efforts are essential and that they will share in the rewards of the organization's success should be paramount.

TABLE I*

	COL (n=16)	LTC (n=20)	MAJ (n=29)	CPT (n=20)
1. Age (yrs)	49+2.9	43.6+2.6	39+2.2	33+3.1
2. Active Commissioned Svc (Yrs)	26+2.5	18.6+2.5	13.3+1.8	5.8+2.7
3. Highest Degree:				
a. MS	37%	31%	20%	15%
b. PhD	63%	69%	80%	85%
4. Military Education				
a. Basic Course	-	-	-	40%
b. Advanced Course	62%	30%	50%	55%
c. C&GS	25%	70%	50%	5%
d. Senior Svc Schools	12%	-	-	-
5. Years in research	9.6+6.7	7.8+5.2	7.5+5	3.9+1.9
6. Reason for military career:				
a. Obligated	75%	70%	50%	40%
b. Job satisfaction	25%	10%	30%	25%
c. Educational opportunity	0	20%	10%	15%
d. Financial	0	0	10%	10%
e. Travel	0	0	0	5%
f. Lack of civilian funds	0	0	0	5%
7. Reason remained on active duty:				
a. Job satisfaction	37%	30%	70%	44%
b. Educational opportunity	37%	30%	10%	17%
c. Financial	12%	20%	10%	22%
d. Security	12%	0	10%	17%
e. Job diversification	12%	0	0	0
f. Lack of civilian jobs	0	0	0	0
8. Promotion criteria:				
a. Satisfied	87%	10%	20%	10%
b. Dissatisfied	0	40%	60%	65%
c. Competitive	87%	30%	30%	10%
d. Unfair to research MSC	0	60%	50%	65%
e. New separate promotion criteria	13%	70%	50%	90%
9. Military funding of civilian education(all or part):				
a. Yes	100%	80%	80%	60%
b. No	0	20%	20%	40%
10. Need separate MSC Research Corps:				
a. Yes	25%	50%	50%	89%
b. No	75%	50%	50%	11%
11. Length of assignment:				
a. Satisfied	100%	70%	50%	47%
b. Dissatisfied	0	30%	50%	53%
12. Effect of changing research assignments:				
a. Detrimental	50%	44%	70%	57%
b. Minimal	25%	33%	20%	28%
c. Enhance productivity	25%	22%	10%	14%
13. Publications:				
a. First author	6.1+6.3	5.3+5.1	9.3+7.4	4.9+5
b. Second author	11.7+11.1	5.6+5.2	9.5+8.0	3.9+3.5
14. % Time performing:				
a. Research	5%	8%	25%	48%
b. Administrative	59%	56%	38%	14%
c. Laboratory management	17%	12%	9%	15%
d. Patient care	3%	2%	11%	8%
e. Consulting	10%	8%	8%	2%
f. Teaching	3%	7%	4%	5%
h. Non-MOS functions	2%	7%	4%	5%
15. % MSC Researchers who have performed research within the AMEDD	75%	86%	81%	70%

*This survey was approved under WBANC Clinical Investigation Protocol 84/78 by the Institution Review Committee. The data obtained and the conclusions drawn from this study do not represent the official views of the Department of the Army or the Department of Defense.

TABLE II

The following questions (a-kk) were ranked in order of preference
(Minimum 1 - Maximum 7)

	COL (n=18)	LTC (n=20)	MAJ (n=20)	CPT (n=20)
a. Satisfied with military	6.1±.83*	5.1±1.1	4.8±1.5	4.8±1.1
b. Identify with military	6.5±.53	5.7±1.5	4.6±1.5	4.3±1.6
c. Participate in military social activities	5.1±.64	4.0±.19	3.2±1.8	2.8±1.7
d. Control over career development	5.8±1.0	4.3±1.5	3.8±1.5	3.5±1.4
e. Sense of belonging to military	6.1±.64	4.5±1.9	4.6±1.4	3.7±1.6
f. Benefit of military to professional growth	6.3±.89	5.8±.93	5.8±1.0	5.2±1.2
g. Likelihood of promotion	2.7±2.7	3.9±2.2	3.8±2.2	4.7±1.8
h. Likelihood of extending beyond obligation	4.1±3.0	4.4±2.1	5.2±1.9	5.2±2.0
i. Likelihood of retiring from the military	6.9±.35	6.3±1.4	6.1±1.1	4.4±2.0
j. Willingness to serve out career at present rank	6.5±1.1	4.5±2.4	4.2±2.3	3.2±2.1
k. Commitment to research	4.4±1.7	4.5±1.9	5.4±1.5	5.8±1.1
l. Commitment to military	6.5±.76	5.7±1.5	5.1±1.4	4.3±1.9
m. Satisfaction with pay	5.8±1.5	4.9±1.7	4.9±1.3	4.8±1.3
n. Satisfaction with coworkers	5.8±1.0	5.6±.75	5.9±1.2	5.0±1.2
o. Satisfaction with supervisors	5.3±1.8	5.0±1.7	5.4±1.3	4.8±1.2
p. Satisfaction with research	5.4±1.1	5.0±1.7	5.5±1.3	4.9±1.7
q. Ability to work on research in your field	6.1±1.1	5.5±1.9	5.8±1.6	5.4±1.5
u. Does conducting research provide opportunity for promotion	5.0±1.4	2.9±1.8	2.9±1.5	3.1±1.7
x. Satisfaction with the need for advanced military education for promotion	5.4±1.4	3.5±2.2	3.1±2.3	2.5±1.6
aa. Importance of being a commander	4.3±2.1	2.3±1.7	2.3±1.7	2.1±1.4
bb. Importance of controlling your own research	5.3±1.0	5.7±1.5	6.0±1.0	5.8±1.1
ff. Satisfaction with special military duties (AOD etc)	5.5±1.4	5.0±1.8	3.9±2.0	4.1±1.8
gg. Knowledgeable about positions within your MOS	5.6±1.4	5.5±1.5	4.2±2.1	3.5±1.6
ii. Control over selection of next assignment	5.6±1.5	5.0±2.0	4.1±1.7	3.7±1.3
kk. Satisfaction with length of assignments	6.1±1.1	5.8±1.6	4.7±1.5	4.6±1.4

*Mean ± SD

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/19 Status: Ongoing

Title:

Evaluation of the Mandibular Staple Bone Plate and the Ramus Frame Implant in the Rehabilitation of the Atrophic Edentulous Mandible.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL F.C. Theisen, DC

Dept/Sec:

Assoc Investigators

Key Words:

Mandibular staple

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Study Objective:

To evaluate the efficacy of two alloplastic implants in the rehabilitation of the edentulous atrophic mandible. Future application will be evaluated for the reconstruction of avulsive traumatic injuries to the mandible and ablative surgical procedures in treatment of pathology in the mandible. Factors to be evaluated include a) the surgical procedure for insertion, b) stability and retention afforded the denture, c) patient function and comfort, d) complications, e) long term followup stability and overall versatility of both implants.

Technical Approach:

All patients selected will be approved by both the Prosthodontic Service and the Oral Surgery Service, WBAMC. Active duty personnel must have a minimum of 12 months remaining prior to anticipated ETS or PCS. Dependents or retired personnel must be residents of the El Paso area and agree to a minimum of two years followup. The patient will have a minimum of 7mm vertical osseous height for the ramus frame and 9mm for the mandibular staple as measured on a lateral cephalometric radiograph. The oral soft and hard tissues will be free of active disease of pathology. The ramus frame implant will be primarily utilized for those patients who are medically contraindicated for general anesthetic. Patients who are candidates for the mandibular staple will have all pre-implant surgical preparation done a minimum of three months prior to placement of the implant. These include alveoloplasty and vestibuloplasty with skin grafting for lowering of mucosal and muscle attachments. Medical assessment of the patient will be accomplished by the Oral Surgery Svc or by WBAMC medical staff when indicated.

The patient will be counselled on the investigational nature of the procedure, to include expected results and possible complications. The patient will be required to sign an agreement concerning his participation in the study and the required followup.

Patients will complete post-operative questionnaires during the six month postop followup visit.

PROGRESS

Currently eleven implants are in place. Progress has been slower this past year. No publications have been completed. One patient has experienced chronic intraoral exposure of a portion of her implant. The implant has remained free of infection and is stable. Surgical repair is planned. No adverse reactions have been encountered.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/02 Status: Terminated

Title:

Lidocaine as an Adjunct to General Anesthesia

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Kochansky, ANC

Dept/Sec: Dept Nursing

Assoc Investigators

Key Words:

Lidocaine

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Study Objective:

To evaluate lidocaine as an adjunct to general anesthesia and its hemodynamic and neurological effects.

Technical Approach:

A clinical research design will be used to study the effects of intravenously administered lidocaine in ASA III-IV patients known to have atherosclerotic cardiovascular disease. Control measurements of cardiac indices (myocardial contractility, heart rate, and myocardial wall tension) expressed as left ventricular stroke work index, cardiac output and pulmonary capillary wedge pressure will be taken prior to induction and at induction and incision. Under local anesthesia, a radial artery catheter, central venous pressure catheter, and a Swan-Ganz catheter is routinely placed as part of the anesthetic in ASA III-IV patients who present for aorto-bifemoral bypass grafting, aortic abdominal aneurysmectomy and carotid endarterectomy patients with severe cardiovascular/pulmonary disease. A control group of patients, selected by random entry, will receive fentanyl instead of lidocaine as per standard practice at WBAMC.

Progress:

Principal investigator no longer at this institution, study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 76/33 Status: Terminated
Title:

Diagnostic Adrenal Scanning with ¹³¹I (NP59)

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T. Brown, MC

Dept/Sec: Nuclear Medicine Svc Assoc Investigators
Key Words:

Adrenal scanning

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Study Objective:		

The purpose of this study is to determine the usefulness of ¹³¹I NP59 in scanning of the adrenal glands. It will be employed for the following purposes: (a) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma, (b) imaging of adrenals in patients who require adrenal venography and are allergic to contrast media, (c) detection of unilateral adrenocortical hypofunction: calcification, metastatic carcinoma, post-venography infarction, etc., (d) detection of functioning adrenal remnant after adrenalectomy for Cushing's syndrome, (e) aid in assessment of adrenocortical steroid therapy.

Technical Approach:

Patients with clinical evidence of adrenal disease will be studied upon referral from the Endocrine Service. Adrenal imaging will be performed after injection of the material to assess the presence or absence of visualization of the adrenal glands, their size and response to suppression therapy.

Progress: The annual review of this protocol was conducted 30 Sep 84. No patients have been entered into this study during FY84. Principal investigator has been reassigned and the study has been closed.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/05 Status: Completed

Title:

The Role of Food Allergy in the Pathogenesis of Migraine Headache

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic

Assoc Investigators

Key Words:

Food allergy; Migraine headache

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Study Objective:

Assess whether skin testing to a battery of food allergens is of value in defining a diet which will cause a decreased frequency of migraine headaches in affected patients.

Technical Approach:

Subjects will be 18 years or older. They will be selected from the population of the Neurology Clinic, WBAMC. They will be judged by one of the investigators to have migraine syndrome. The nature, the purpose, and proposed benefits of the study will be explained to them. If they are agreeable, the following will be done: (1) Any medications being used for chronic migraine prophylaxis will be discontinued. (2) They will be given a supply of medication for acute migraine attacks. (3) They will report to the Allergy Clinic where the following will be performed:

- a. A history regarding possible food provoked migraine.
- b. Prick puncture testing on the back to 75 common foods.
- c. A diet will be prescribed avoiding those foods which are positive on skin testing (2 mm wheal greater than control).
- d. A small blood serum specimen (5 ml) will be collected and frozen for later use if required.

If there are no positive skin tests, the patient will be placed on a corn, egg, milk, wheat free diet. The duration of the diet will be eight weeks. The patients will record symptoms and medications on the diary sheets. Each four weeks the patients will meet with one of the investigators. At the end of eight weeks those who appeared to have had a positive response, that is complete absence of attacks or a greater than 50 percent diminution, will remain on the diet.

Those patients will then undergo a double-blind challenge supervised by one of us. All of the materials for the challenges will be prepared by the other investigator and his staff. The challenge shall be performed in the following manner. Patients will be given a group of opaque capsules containing placebo or freeze-dried foods. The foods chosen will be according to what was eliminated. Interspaced with the foods will be capsules containing placebo (lactose). The maximum amount of challenge food given in one day will be 8 gms. They will take these capsules on a daily basis. This diet challenge period will be individualized for each patient, and may vary in duration. Patients will continue to complete the diary sheets and be seen every four weeks.

Criteria for evaluation of the results will be:

- a. Definitely positive: Significant relief of migraine attacks and positive challenges.
- b. Possible positive response: One of the challenges positive, one negative, diet trial yields relief.
- c. Equivocal placebo effect: Diet trial yields good response in relief of headaches; challenges are negative.
- d. Negative: No relief with the diet trial.

Progress:

Eighty-three patients were included in the study with no adverse effects. Study was completed and a manuscript has been submitted for publication.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/12 Status: Terminated
Title:

A Novel Method of Hyposensitization Therapy with Russian Thistle Antigen

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators
Key Words:

Hyposensitization; Russian thistle antigen

Accumulative MEDCASE Est Periodic
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Study Objective:

To determine if oral administration of Russian Thistle pollen in a pharmacologically modified release form will be capable of: (a) Demonstrating immunologic changes that are comparable to standard parenteral allergen immunotherapy. (b) Demonstrating in a physiologic test, such as nasal provocation, evidence of lessened reactivity to allergen.

Technical Approach:

Thirty adult allergic patients, who are significantly sensitive to Russian Thistle allergen by history and skin testing, will be the subjects for this protocol. The nature and purpose of this study will be explained to them. The study will be conducted from December to March, when ambient Russian Thistle pollen is not present in El Paso.

The subjects will report to the Allergy Clinic. Prior to the initiation of therapy, the subjects will have:

- a. Titrated prick-puncture skin tests performed (3mm wheal end point).
- b. 5 ml blood taken to measure specific serum IgG, IgM and IgE antibodies to Russian Thistle allergen.
- c. Nasal sensitivity to Russian Thistle allergen determined by nasal provocation (doubling of nasal airway resistance as end point).

The patients will be given capsules containing specifically prepared Russian Thistle allergen. This material will be lacquered to avoid digestion and dissolution in the acid media of the stomach. The schedule on a daily basis: 0.15, 0.30, 0.60, 0.90, 1.20, 1.60, 1.90, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0, 9.0, 12.0, 15.0, 20.0, 25.0, 30.0, 40.0, 50.0 mg.

50 mg will be given weekly as a maintenance dose for four more weeks. After this total schedule, the measurements made prior to therapy will be repeated. The results will be analyzed by paired "t" testing of the mean responses.

Progress:

Principal investigator resigned from the Army, no progress reported. Study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/38 Status: Completed

Title:

The Development of Subsensitivity to Atropine

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl

Assoc Investigators

Key Words:

Atropine; Asthma

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OMA Cost:

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Study Objective:

To determine if repeated use of atropine sulfate as a bronchodilator, by the inhalant routes, leads to development of subsensitivity.

Technical Approach:

Twenty adult asthmatic patients will be selected at random from the Pulmonary and Allergy Clinics at WBAMC. The nature and purpose of the study will be explained. On the first day of the experiment they will be tested at the Pulmonary Function Lab according to the following protocol:

- a. 24 hours without oral bronchodilators
- b. Baseline pulmonary functions consisting of conventional spirometry, flow volume loops, and plethysmography.
- c. Inhalation of atropine sulfate 2 mg by nebulizer.
- d. Repeat pulmonary function.

After this the patients will be instructed in the use of a home nebulizer. They will use atropine sulfate 2 mg by nebulizer three times a day for 14 days. At the end of the period, the patients will undergo the same testing as on the initial day. If there is a decrease in response, then ten subjects will be retested after inhalation of 0.5 mg atropine and ten after inhaling 1.0 mg atropine, in addition to the previous 2.0 mg.

Analysis will consist of t-testing of the mean response on each occasion. In the ten subjects of each incremental group, comparison will be made to ascertain which increment, if one is required, to restore responsiveness to the original testing level.

Progress:

Presented at the Carl W. Temple Symposium, Fitzsimons AMC in January 1984. Manuscript for publication is in preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/39 Status: Terminated

Title:
The Usefulness of NonAcetylated Salicylates in the Treatment of
Inflammatory Disease in Patients with Aspirin Idiosyncratic Asthma.

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl Assoc Investigators
Key Words:

Salicylates; Asthma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine if non-acetylated salicylates can be used safely in the treatment of aspirin-idiosyncratic asthmatics with inflammatory disease.

Technical Approach:

Thirty patients with a history of aspirin idiosyncrasy will be selected from the Pulmonary and Allergy Clinics of WBAMC. The nature and purpose of the study will be explained to them. They will report to the Pulmonary Function Lab on four occasions. They will be tested according to following protocols. Measured pulmonary functions will be conventional spirometry and flow volume determinations on each occasion.

DAY 1	Day 2	Day 3	Day 4
<u>Placebo</u>	<u>Aspirin</u>	<u>Disalcid</u>	<u>Trisilate</u>
1 cap	32 mg	250 mg	250 mg
2 cap	64 mg	500 mg	500 mg
3 cap	128 mg	750 mg	750 mg
4 cap	325 mg	1000 mg	1000 mg

The patients will not take oral bronchodilators for 24 hours except for corticosteroids. They will be managed by inhaled bronchodilating agents. Each dose will be spaced 30 minutes apart. All medications will be given in identical opaque white capsules, and the patient will be blinded as to the contents of these capsules.

A significant test for each person will be a fall in one second forced expiratory volume greater than twenty percent of predicted FEV₁, over the fall during the placebo challenge. Any patient who develops clinical symptoms will have their bronchoconstriction reversed. Any subject whose aspirin challenge is negative will be excluded from the study. Each testing will be compared to the placebo day, in terms of possible positive responses.

Specifically, patients will not be entered unless their FEV₁ is greater than eighty percent of predicted at the onset of the study, and patients who develop greater than a twenty percent fall in FEV₁ will be eliminated from the study at that point.

Progress:

Principal investigator has resigned from the Army, no progress reported. Study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/58 Status: Terminated
Title:

The Prevalence of Antibiotic Tolerant Staphylococcus Aureus in
Nasal Cultures of Different Adult Population Group

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Frank J Baker, MC

Dept/Sec: Dept Medicine, Infect Dis Assoc Investigators
Key Words:

Staphylococcus

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To perform an epidemiological survey of Staphylococcus aureus tolerance from isolates not causing clinical infection and determine prevalence rates in different adult population groups.

Technical Approach:

Three population groups consisting of 100 individuals in each group will be studied.

Normals consisting of two subpopulations. Young adults consisting of a defined population, i.e., active duty personnel billeted on post. Older adults consisting of a defined population, i.e., personnel in Health Services Command. This group would be composed of individuals free of chronic disease on no medication or antibiotic therapy.

Outpatients on antibiotics. Young adults from the Dermatology Acne Clinic. Older adults from the Pulmonary Clinic, patients with chronic obstructive pulmonary disease on cyclical antibiotic therapy.

Population with a high prevalence of staph nasal carriage. Renal dialysis and insulin dependent diabetic patients. Hospital personnel. Nasal swabs with culturettes will be obtained from each individual.

(1) All nasal swabs will be streaked on sheep blood agar (SBA). Identification of staph aureus will be by standard methods as per the Manual of Clinical Microbiology, i.e., colonial morphology gram stain.

(2) MIC will be performed in duplicate by standard methods as per the Manual of Clinical Microbiology. After primary inoculation and identification of an organism as staph aureus:

(a) A log phase, four hour growth of the organism will be prepared in Mueller-Hinton Broth (MHB). The inoculum will be standardized to a 0.5 McFarland and a 1/200 dilution prepared. Colony counts will be performed on each inoculum with a desired final concentration 1 or 2×10^5 organisms/ml.

Conclusions: If the prevalence rates were significantly different among the study population groups, the contribution of various epidemiological factors could be determined. If the prevalence rates of tolerant organisms were less than those causing clinical infection, the question of increased virulence and microbiological change of the organism from a colonizer to an invasive form would be raised. Conversely, if the prevalence was equal to or greater than those causing clinical infection, the clinical importance might be lessened for this phenomenon.

If in subsequent studies tolerance was found to be therapeutically important, i.e., necessitating higher dosages or different antibiotics not standardly used for staphylococcal infections, this prior identification of epidemiologic factors might aid in initial selection pending further characterization of the organism. By having identified those individuals with high prevalence rates of tolerant organisms and at increased risks for clinical infections with those organisms empiric selection of treatment might be facilitated.

Progress:

Principal investigator has been transferred with no report of results. Project is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/65 Status: Terminated

Title:

Utility of Furosemide in Early Oliguric Renal Failure. Part of a Multi-center study.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ A. Henry, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Furosemide; Renal failure

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Study Objective:

A randomized study of furosemide effect on the outcome of oliguric acute renal failure. Can this diuretic convert a patient with oliguric acute renal failure to non-oliguric acute renal failure

Technical Approach:

Patients with renal oliguria will be considered for this study. Non-oliguric patients will also be included. However, the patients should not have post-renal obstruction, and if obstruction is suspected on clinical grounds, a complete workup will be done. In addition, pre-renal factors contributing to the renal failure, such as hypotension, volume depletion and congestive heart failure, will be corrected. Any patient with diminished hearing as determined clinically by questioning will be excluded from the study. Also any patient that experiences transient hearing loss after the first furosemide dose will be excluded from subsequent doses. Absence of administration of furosemide or other diuretic agents within the previous twelve hours will be a criteria for entry as will serum creatinine greater than 2.0 mg/dl.

There will be two patient groups, furosemide and saline placebo, as determined by the use of a random numbers table. Consecutive patients assigned an even number from the random numbers table will receive furosemide. Patients assigned an odd number will receive saline. The random numbers table will be employed by using horizontal rows.

Progress:

No patients have been entered into this study. Recommend termination.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/02 Status: Completed
Title:

Comparison of Bone and Joint Scans in Patients with New Onset
Polyarthrititis or Polyarthralgias

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Mark W. Nelson, MC

Dept/Sec: Assoc Investigators
Key Words:

Polyarthralgia

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

The detection of inflammation in asymptomatic or arthralgic joints is useful for objective documentation of organic disease in medical-legal or Workman's Compensation cases and to determine early in the course of a patient the exact distribution of involved joints, therefore aiding in diagnosis (Rheumatic joint disease is classified on the basis of joint distribution). A sensitive although nonspecific test to detect such subclinical involvement would be useful. We will compare Tc99m MDP scanning reflecting metabolic activity of bone with Tc99mO₄ which reflects blood pool activity and is cheaper and simpler to obtain.

Technical Approach:

Patient population: New onset polyarthrititis or polyarthralgia in adults (symptoms less than six months).

Procedures:

I.a. A rheumatologist will make a clinical joint chart on patients noting joints where objective arthritis is present. This will be done prior to scanning.

b. The patient will then receive both scans, which will be done in the Nuclear Medicine Service under the supervision of Nuclear Medicine staff physicians. The scan will be interpreted without knowledge of the clinical joint chart and independently of each other.

II. a. The number of clinically involved joints will be compared to involved joints on bone and joint scans. A positive bone scan will be considered to be a true-positive of increased metabolic bone activity and a positive joint scan will be considered a true-positive reflecting increased flow to a joint. This applies only to activity in joint area.

b. The previously identified joints on scan will be followed to determine the long-term significance of a positive scan.

PROGRESS: A total of twenty-five patients were entered into the study with no adverse reactions recorded. A manuscript is in preparation detailing results.

From this data, an assessment of percentages of appropriately drawn and utilized serum gentamicin levels will be determined. A comparison of overall morbidity and mortality will be made between the group in which the procedure was used appropriately and the group in which it was not.

The second part of the study will be prospective and 12 months in duration. A list of patients receiving gentamicin will be maintained by the pharmacy. This list will be reviewed daily and those patients meeting the criteria will be entered into the study..

Having obtained baseline data and identified problem areas from the retrospective review, an educational program will be instituted just prior to initiation of the 12 month prospective study. This will consist of lectures on gentamicin pharmacokinetics, toxicity and the appropriate use of gentamicin levels. The results of the retrospective review and problem areas will be included. At two to three month intervals an update of the ongoing prospective study will be reviewed with continuing problem areas emphasized. This will be presented in depth to house staff and staff during one hour lectures, and informally to ward personnel in 30 minute in-services. One to one teaching will occur in those instances where physicians are not using or have inappropriately used gentamicin levels.

At the end of the 12 month study period the data from the retrospective and prospective study will be compared for statistically significant differences.

7. METHODS, DEFINITIONS:

I Patients:

- a. The criteria for inclusion/exclusion has been outlined.
- b. Patients will be classified into three categories based on the severity of underlying disease by the criteria of McCabe¹⁶.
- c. Rapidly fatal disease: to be utilized solely for patients with acute leukemia or blastic relapse of chronic leukemia.
- d. Ultimately fatal disease: Arbitrarily based on the severity of the underlying disease rather than the specific diagnosis. The disease is likely to prove fatal within the next five years. Patients with carcinoma, with proved metastases, myeloma, lymphoma, aplastic anemia, severe renal failure and liver disease with spontaneous coma or bleeding esophageal varicies to be included in this group.
- e. Non-fatal: The underlying disease is considered unlikely to be fatal within the next five years.

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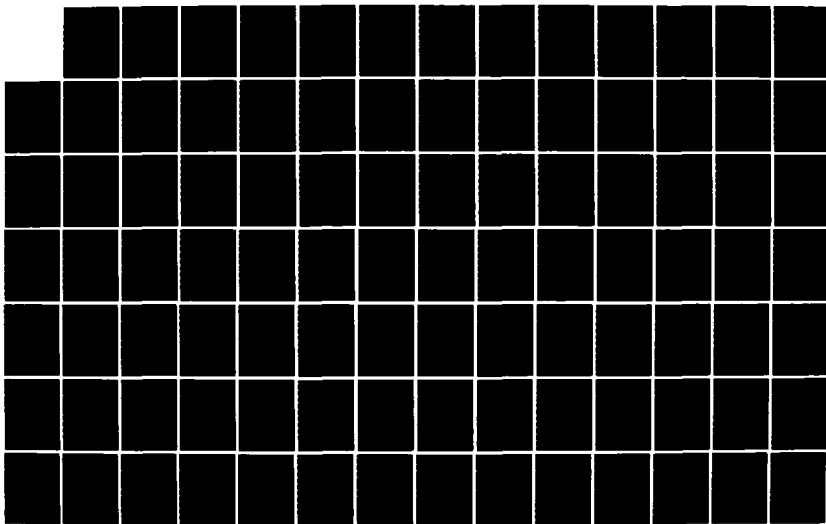
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At the end of the 12 month study period the data from the retrospective and prospective study will be compared for statistically significant differences.

7. METHODS, DEFINITIONS:

I Patients:

- a. The criteria for inclusion/exclusion has been outlined.
- b. Patients will be classified into three categories based on the severity of underlying disease by the criteria of McCabell⁶.
- c. Rapidly fatal disease: to be utilized solely for patients with acute leukemia or blastic relapse of chronic leukemia.
- d. Ultimately fatal disease: Arbitrarily based on the severity of the underlying disease rather than the specific diagnosis. The disease is likely to prove fatal within the next five years. Patients with carcinoma, with proved metastases, myeloma, lymphoma, aplastic anemia, severe renal failure and liver disease with spontaneous coma or bleeding esophageal varicies to be included in this group.
- e. Non-fatal: The underlying disease is considered unlikely to be fatal within the next five years.

II. Morbidity

a. Nephrotoxicity

A rise in serum creatinine of 0.5 mgm% or greater if initial level is less than 3 mgm%, or a rise in serum creatinine of 1 mgm% if initial creatinine is more than 3 mgm%.

b. Ototoxicity - gross abnormalities, i.e. deafness, ataxia or nystagmus occurring during therapy. Audiometry and aloric testing will not be performed.

c. Length of hospital stay.

III Mortality:

All deaths which occur within 7 days of onset of bacteremia will be considered due to bacteremia unless a 2nd usually lethal event, not associated with or precipitated by bacteremia occurred and there is strong clinical evidence of recovery from the episode of bacteremia. Adapted from McCabes definition¹⁶.

IV Use of gentamicin levels:

a. Defined as:

Therapeutic - peak serum concentration of 4-12 ug/ml

Sub-therapeutic - peak serum concentrations of less than 4 ug/ml

Toxic - Peak serum concentration of more than 12 ug/ml or trough serum concentrations more than 2 ug/ml

b. Time of sampling (correctly drawn)

Peak - drawn 30 minutes after an IV infusion

Trough - drawn just prior (within 30 minutes) of IV infusion

c. Use of levels obtained as correctly drawn peaks/trough pairs will be classified as appropriate if:

- (1) The peak and trough is in the therapeutic range and the dose is not changed.
- (2) Peak is more than 12 ug/ml and the dose is decreased.
- (3) Peak is less than 4 ug/ml and the dose is increased.
- (4) Trough is more than 2 ug/ml and the interval is increased.
- (5) Any combination of the last three.

V. Data analysis.

a. At the conclusion of the retrospective study, the percentage of patients having appropriately drawn and utilized levels will be tabulated. Comparisons will be made of these patient categories, defined by severity of underlying disease, who had serum gentamicin levels drawn and utilized appropriately and those who did not. The influence of inappropriately drawn gentamicin levels on overall morbidity and mortality as defined will then be assessed.

b. At the conclusion of the prospective study the percentage of patients who had appropriately drawn and utilized levels will be compared to the retrospective group. If there is a significant difference between the prospective and retrospective group, the influence on overall morbidity and mortality will be assessed. The influence of the education program can then be measured.

Progress:

Principal investigator has been transferred with no progress reported. The study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/18 Status: Terminated

Title:

The Use of a Combination of Isoelectric Focusing, Inhibition Radioautography and Enzyme Labelling to Determine Cross-Reacting Allergens.

Start Date:

Est Comp Date:

Principal Investigator:
LTC L.E. Mansfield, M.D.

Facility:

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Cross-reacting allergens

R.F. Frederick, Ph.D

Accumulative MEDCASE Cost

Est OMA Cost:

Periodic Review Results

Study Objective:

To determine if a novel approach using a combination of isoelectric focusing and radioautography and enzyme labelling will be useful in determining cross-reacting allergens of pollen extracts.

Technical Approach:

1. Technical consideration for optimum analytic isoelectric focusing of pollen extracts will be worked out for our laboratory.
2. After this stage has been accomplished, a technique for electroblotting the separated protein bands on paper will be utilized. This procedure will end any significant diffusion of the proteins and make possible Step 3.
3. The paper will be overlaid with human allergic serum specific to the pollens involved. The paper will have been previously treated so that nonspecific binding of serum globulins on the paper cannot occur. After the overlaying and antigen-antibody reaction, the paper will be washed to remove any serum protein not immunochemically bound to the allergen proteins. The next step will be a second overlay with radiolabeled anti-human IgE (FC Specific). This will be followed by another gentle washing. The paper will be dried and placed on an x-ray film for radioactive exposure of the film. Lines of interest should develop where human IgE antibodies have bound to the allergen proteins.
4. In the enzyme labeling technique anti-human IgE chemically bound to horseradish peroxidase will be used as the

marker rather than the radiolabel. The bands will be subjected to a colorimetric reaction catalyzed by enzyme conjugate. The intensity of the reaction will be read by spectrophotometric methods.

5. In this step the human allergic sera will be preincubated with an allergen extract suspected of containing cross-reacting proteins to the allergen extract, electrophoresed and transferred to paper. The incubated sera will be used in the same manner as described in Steps 3 and 4.. Absence or diminution of intensity of the bands on the x-ray film will occur if the allergen extract contains proteins which cross react with allergens in the first extract.

Progress:

Both investigators have departed this institution with no progress reported. Terminated.

Detail Summary Sheet

Date: 1 Oct 84	Prot No: 82/20	Status: Completed
Title: An Investigation Into Possible Bronchoconstrictive Reflexes Arising with Gastric Distention in Asthmatic Subjects		
Start Date:	Est Comp Date:	
Principal Investigator: LTC L.E. Mansfield, MC	Facility:	
Dept/Sec: Dept Medicine	Assoc Investigators	
Key Words: Gastric Distention		
Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To discover if gastric distention causes a bronchoconstrictive response in asthmatic subjects. To determine if pretreatment with atropine ablates this response.

Technical Approach:

Twenty adult asthmatic patients will be selected at random from the allergy immunology clinic population. They will come to the clinic at 0800 (having omitted their morning bronchodilators if tolerated). Total respiratory resistance will be measured by the method of forced oscillations and then conventional spirometric and flow-volume determinations will be performed.

Each subject will drink 20 oz. of water. All pulmonary functions in the same order as at baseline will be repeated. The subject will continue drinking water until he/she experiences the sensation of fullness (as after eating a bit too much). Pulmonary function tests will be repeated.

If the airway response to gastric distention, as measured by pulmonary functions, is compatible with bronchoconstriction, then the five patients in whom this response was most dramatic will be reinvestigated to determine if atropine will inhibit this reaction. These patients will report on a second day at 0800 omitting bronchodilators, if possible. Baseline pulmonary functions will be determined, two mg. atropine sulphate will be delivered to the patient by aerosol nebulization. A post-atropine baseline will be established 15 minutes after this treatment. The same procedure as outlined above will be followed concerning water ingestion and pulmonary function determinations.

The results will be analyzed by appropriate parametric and nonparametric statistics.

Progress:

Nineteen patients successfully completed this protocol. Statistical analysis revealed evidence of very mild bronchoconstriction upon gastric distention. Manuscript reporting results is in preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/22 Status: Ongoing

Title:

Use of Topical Steroid Cordan Tape (Fluorandrenolide) in the Management of Skin Reactions

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ S. Ting, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Fluorandrenolide

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine whether locally applied cordan tape suppresses the histamine release, eosinophil migration and ultrastructural changes of mast cells in human allergic skin reaction.

Technical Approach:

Ten volunteers from the Allergy Clinic will be skin tested with ragweed and 48/80. Injections will be 0.02 ml of ragweed 1000 PNU/cc and 48/80. Skin blister technique will be employed and cordan tape placed over both forearms for 24 hours, then skin biopsy to determine measurement of histamine release.

Progress:

Principal investigator has been unable to solicit volunteers during the last reporting period.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/01 Status: Terminated
Title:

A Comparison of Ga-67 Citrate Tc99m MDP and In-111 Labeled White Blood Cells for the Diagnosis of Osteomyelitis

Start Date: Est Comp Date:
Principal Investigator: Facility:
LTC T. Brown, MC

Dept/Sec: Dept Medicine/Nucl Med Assoc Investigators
Key Words:

GA-67 Citrate; Tc99m MDP; In-111 Labeled White Cells

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To compare the sensitivities of Ga-67 citrate, Tc MDP and I-111 WBC in diagnosing osteomyelitis and to determine whether differences in the relative labeling of the radiopharmaceuticals can be used to increase the specificity of the scintigraphic diagnosis of osteomyelitis.

Technical Approach:

New Zealand white rabbits will be anesthetized with 0.8cc of innovar and 0.2cc of atropine. The right hindleg will be shaved and an 18 ga needle introduced into the right femur. One tenth cc of sodium morrhuate and 0.1cc of a suspension of Staphylococcus aureus will be introduced. At the end of four weeks, after appropriate scanning, bacterial culture of bone marrow will substantiate the diagnosis of osteomyelitis. Twenty-one rabbits with presumed osteomyelitis will be divided into groups of three rabbits each. Every two days a group will be imaged with Ga-67 citrate and Tc MDP and then sacrificed. The bone will be cultured to prove the existence of osteomyelitis. Another group of twenty-one rabbits with presumed osteomyelitis will be treated in a like manner except I-111 WBC and Tc MDP will be used for imaging. Images on film will be read by investigators. The first positive image after initiation with osteomyelitis will be noted for each radiopharmaceutical. A comparison then will be made for sensitivity of each agent for the early states of osteomyelitis. In addition, the images on the computer will be processed to compare relative quantity of each radiopharmaceutical at the site of osteomyelitis.

Progress:

Principal investigator was transferred and the study has been closed. No patients were entered this FY.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/08 Status: Terminated

Title:

The Evaluation of Two Central Venous Lines Inserted Through One Venipuncture Site

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ B.L. Feaster, MC

Dept/Sec: Dept Medicine

Assoc Investigators

Key Words:

Venous lines

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

Evaluate the use of the insertion of two central venous lines through one central venipuncture site as a viable alternative to the critically ill patient who requires several central venipunctures for central intravenous access. This technique would reduce the number of venipunctures and concomitant morbidity.

Technical Approach:

The study will include 200 patients consecutively admitted to the Medical Intensive Care Unit of WBAMC, requiring central venous lines. They will be randomized on an alternating basis into study group (two central lines through one venipuncture) and control group (one central line through one venipuncture).

Progress:

Principal investigator has been transferred and the study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/10 Status: Completed
Title:

An Investigation of Immunological Reaction to Human Serum Albumin

Start Date: Est Comp Date:
Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Allergy/Immunology Svc Assoc Investigators
Key Words:

Immune reaction; HSA

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine whether allergy patients receiving injections of allergy extracts containing human serum albumin develop evidence of IgE or IgG antibodies directed towards human serum albumin.

Technical Approach:

Evidence of IgE reactivity will be sought by performing intradermal skin tests with the diluent containing 0.03% HSA. These will be performed on consenting individuals who have received injections of allergy extracts from the Army Central Extract Laboratory for a period of one year. Patients will be asked to refrain from antihistamines for 3 days before the skin tests are performed at the same time on the opposite arm. The tests will be placed on the lateral aspect of each upper arm. Wheal and flare for both will be measured and recorded. Any patient who develops a wheal and flare reaction with the injection of the diluent will have blood drawn to perform a RAST and blocking antibody measurement against human serum albumin. In addition, every tenth patient who is skin tested will have blood drawn for specific IgG and IgE antibodies directed towards human serum albumin.

The presence of specific IgG antibodies will be assessed by the performance of a double antibody precipitation test in which the same preparation of human serum albumin employed in the diluent will be radioiodinated, added to a dilution of the patient's serum, to which, after appropriate incubation, will be added an anti-human IgG to precipitate the patient's IgG and any combined radiolabeled human

serum albumin.

RAST: Radioallergosorbent testing will be performed with HSA bond to cellulose disks by the cyanogen bromide technique. Commercial I-125 antihuman IgE will be employed. Positive control will be provided by heterologous antihuman HSA and radiolabeled antisera directed towards the IgG of that species.

Progress:

Collaborative study with FAMC. Data was sent to FAMC. Project is complete.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/19 Status: Ongoing

Title:

Characterization of Bronchodilator Activity of Inhaled Dyphylline

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

CHANGE INVESTIGATOR TO LTC A.L. SHELTON, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Dyphylline

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine if dyphylline can be used as an inhaled bronchodilator and to characterize the response for possible clinical application.

Technical Approach:

Ten adult asthmatic, nonpregnant, and not of child bearing potential subjects will be entered into this study. Their asthma will be sufficiently moderate so that they can withhold their usual morning dose of bronchodilators. They will report to the Allergy Clinic at 0800. Baseline pulmonary functions, including conventional spirometry, flow volume curves, and total respiratory resistance will be measured. Serum will be drawn for a theophylline level. The subject will then inhale to completion through a nebulizer (Devilbis 646) with a pulmonaid compressor a solution containing 1 mg/kg of dyphylline (with normal saline added to make a 5 ml total volume). Patients will be observed for any possible adverse reactions such as tachycardia, nausea, or headache. Pulmonary function will be remeasured immediately after finishing the treatment, and at 15, 30, 45, 60, 90, 120, 180, 240 minutes post-treatment. A repeat theophylline level will be obtained at 30 minutes post-treatment. In as many individuals as technically possible, determinations will be continued for 300, 360, 420, and 480 minutes. Where this will not be possible, a portable peak flow meter will be given to the subject to record PEFr at these time intervals. At any point where the subject notices distress, or in the opinion of the physicians further bronchodilation is indicated, then inhaled albuterol will be used.

In each of the subjects, the same procedure will be repeated at a dose of 3 mg per kg, 5 mg per kg, and 7 mg per kg. Rather than randomize the sequence of doses, it is the investigator's opinion that for the safety and comfort of the volunteers, this progressive dose exposure is more prudent. Therefore, on three other separate individual occasions, the same methodology and parameters will be used to determine the response to these larger doses.

It is estimated that the nebulization system used will deliver between 5-10 percent of actual dose to the patients, so that the effective delivered dose will be 0.1, 0.3, 0.5, 0.7 mg/kg. The usual systemic oral or parenteral doses are between 5-10 mg/kg q6-8h for dyphylline.

During each session subjects will be closely observed for tolerance of the treatment, the side effects and adverse reactions as described above. The unique taste of dyphylline makes the use of a placebo of doubtful value. Data for the expected response of a group of moderate asthmatics to placebo (saline inhalation) is available in the medical literature.

Dose response and durations of effect curves will be plotted.

Progress:

No patients have yet been entered. The study will continue with a new principal investigator.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/20 Status: Completed

Title:

Tissue Distribution in Pregnant Lactating Sheep of the Six Most Commonly Ued Radiotracers

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT M.A. Yedinak, DO

Dept/Sec: Dept Medicine/Nuc Med

Assoc Investigators

Key Words:

Radiotracers

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine tissue distribution patterns of six of the most commonly used radiopharmaceuticals in pregnant sheep. Second, to determine, if possible, the effects of Delta-9-tetrahydrocannabinol (D-9-THC) on tissue distribution and relative perfusion. Third, to calculate the percentage of dose of radiotracer to breast, placenta, and fetal tissue.

TECHNICAL APPROACH:

Twelve pregnant sheep at approximately 131-143 days' gestation will be studied in six sets of two sheep/set. Six different radiopharmaceuticals will be used, one for each set of two sheep. Within each set sheep will be imaged with and without Delta-9-THC. The following is a set by set design.

SET I (99mTc & PYP)

Sheep #1 and 2 will be injected with 99mTc and PYP in a normal resting state and first pass and MUGA studies will be performed. A computer generated first pass and EF (ejection fraction) will be calculated. The breasts, placenta and fetus will be imaged for blood pool activity and a time activity-curve will be obtained. This data should supply relative perfusion to the fetus via the placenta. Specimens will be taken of serum to determine concentrations of radiotracer. The sheep will be studied one day before and one day after catheter placement (see Protocol 82/57) and immediately before and 30 minutes following a 0.5 mg/kg dose of Delta-9-THC. EFs and flows will be compared for drug effects on ejection fraction and placental perfusion.

SET II (99mTc-GLHP)

Sheep #3 and 4 will be injected with GLHP and tissue distribution patterns for brain, breast, renal, placenta and fetal areas will be observed at the same time designated in Set I.

SET III (99mTc MDP)

Sheep #5 and 6 will be injected during the control periods with MDP (Bone Agent), and two hours later imaged for distribution to breast, placenta and fetus. They will be injected with MDP one hour post-injection with 0.5 mg/kg of D-9-THC and imaged.

SET IV (mmTc DISI)

Sheep #7 and 8 will be injected with DISI (hepatobiliary agent) and breast, placenta, fetus and liver/spleen will be imaged at the control times. They will be injected with DISI 30 minutes following injection with 0.5 mg/kg of D-9-THC and imaged. Blood will be drawn for estrogen and progesterone levels.

SET V (99mTc-Folate)

Sheep #9 and 10 will be injected with tracer-labeled folate to determine normal distribution patterns for this tracer. Particular interest will be focused on breast, placenta and fetus. Depending on control results, they will be injected with radiolabeled folate either before or following injection with D-9-THC and imaged as before

SET VI (Ga-67 Citrate)

Sheep #11 and 12 will be injected with gallium citrate and imaged at 24, 48, and 72 hours post-injection. Areas of interest will be the breast, placenta and fetus. Breast milk samples will be taken at 24, 48 and 72 hours and radiotracer concentrations determined. Upon sacrifice of the experimental animals, specimens will be taken of breast, placenta, cord, and fetus to be used for determination of radiotracer concentrations and autoradiographs will be made to localize tracer accumulations.

If possible, breast milk will be obtained in the other group for radiotracer quantitation. In each group, if resources permit, references at the 0.25 mg and 1.0 mg/kg doses (see protocol 82/57) will be studied.

PROGRESS:

Completed and combined with WBAMC Protocol 83/49.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/24 Status: Completed

Title:

Measurement of Salivary Histamine

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ S. Ting, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Salivary histamine

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine whether salivary histamine levels will provide an additional modality for recognition of allergic patients.

Technical Approach:

1. Collect saliva from 100 non-atopic individuals
2. Collect saliva from 100 atopic individuals
3. Collect saliva from 100 atopic individuals on immunotherapy
4. Determine salivary histamine levels.
5. The volunteer will be asked to rinse the mouth with lemon juice, 1 teaspoonful for 1 minute and then spit out the saliva into a container provided.

Progress:

Forty patients were entered with no adverse reactions. The study is complete, and we are awaiting the analysis of histamine.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/36 Status: Terminate

Title:

Prospective Study of Clinical, X-Ray, Histologic, Scintigraphic and Microbiological Characteristics of Diabetic Feet

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ John Baker, MC

Dept/Sec: Dept Medicine/Infectious Dis Assoc Investigators

Key Words:

Diabetic feet

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To correlate specific x-ray, scintigraphic, clinical and microbiologic characteristics with each other and with the histology of the diseased diabetic foot so that clinicians may better manage their patients.

Technical Approach:

The technical approach is very lengthy and may be reviewed in the Dept Clinical Investigation

Progress:

Principal investigator transferred. No patients were entered into this study, and the study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/40 Status: Terminated

Title:

Use of Protein Infusion to Decrease Absorption of Chemical Moieties from the Serum and to Establish a Working Model for Protein Therapy: A Pilot Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ G.D. Griffin, MC

Dept/Sec: Assoc Investigators

Key Words:

Protein infusion

MAJ A.W. O'Brien, VC

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

Use of protein infusion to decrease absorption of chemical moieties from the serum and to establish a working model for protein therapy.

Technical Approach:

In this pilot study dogs will be used as the model. After determining the normal protein levels, dogs will be overdosed on ASA to a level of 240 mg/kg. Serum toxic level will be a guide to use as baseline. Determination of ASA and protein level in serum and urine. Levels will be drawn every 15 minutes for four hours to determine baseline and normal progression of the serum ASA and protein levels. Other parameters measured are osmoles SMA-6 ph in urine and serum and respiratory rate, heart rate, and blood gas. After determining base parameters as above the animals will be re-dosed to 240 mg/kg and will be given continuous IV protein infusion of dog albumin. The above serum levels will then be repeated to determine if the exogenous protein changes the concentration of the protein bound drug in the serum, as well as in the tissues. The time interval between baseline determination and redosing depends on the above results - ie., when serum ASA levels are zero redosing occurs. Urine samples will be obtained by catheterization. Sex of the animal should not matter. Each experiment is anticipated to last about 16 hours from beginning to end, and there will be a total of three sixteen hour runs. The three sets of data will then be analyzed and compared.

PROGRESS:

One experiment was completed. Transfer of Veterinarian and principal investigator precluded further studies.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/42 Status: Completed

Title:

The Incidence of Papain and Bromelain Hypersensitivity in an Allergic Population

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Papain/Bromelain hypersensitivity

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine the degree of papain and bromelain sensitization in an allergy clinic population; to determine the clinical relevance of such sensitization.

Technical Approach:

Volunteers from the Allergy-Immunology Clinic who have a 3+ or 4+ wheal and flare response to prick/puncture cutaneous allergy testing with 1 mg/ml papain or bromelain will be entered into this study. Patients who believe they have had a life threatening reaction from papain or bromelain ingestion will not be studied. Pregnant patients nor potentially pregnant patients will not be studied. Patients with serious medical problems will be excluded from the study.

Patients will received a capsule containing papain/or bromelain in an amount used to tenderize an average 8 oz steak, depending on skin test results. If both are positive a second open challenge day will be performed. They will be observed for one hour post-ingestion and given a diary sheet to take home for recording any unusual symptoms over the next 24 hours. If signs or symptoms apper the subject will enter a single blinded phase of the study. They will return on four to six occasions to receive a capsule. This capsule will contain either papain/bromelain or placebo. This procedure will be performed in a single blind fashion. Finally, if any of the symptoms reported are vague, a similar double blind challenge will be instituted instead of single blinding.

Vague symptoms are considered subjective changes such as feeling tired, aching, etc. In general signs and symptoms likely to be observed include urticaria, asthma, rhinitis, headache, nausea, diarrhea and vomiting. Since these subjects have not been avoiding tenderizer in their day to day life, it is highly improbable that a more severe previously undetected reaction will occur. The results will be analyzed to gather the following data: Prevalence of sensitization to pain and bromelain in an allergy population; whether people sensitive to one tenderizer are more likely to be sensitive to both; whether this sensitization is clinically meaningful; what is the frequency of clinically meaningful sensitization?

PROGRESS:

Study is completed, 412 patients entered into the study with no adverse effects. A manuscript on the results has been submitted for publication.

Detail Summary Sheet

Date: 1 Oct 84 Prot No 83/43 Status: Completed
Title:

The Incidence of Immediate and Prolonged Bronchoconstriction
Following the Use of Metered Dose Inhaler Beta Adrenergic Agents

Start Date: Est Comp Date:
Principal Investigator: Facility:
Ms Josephine Yarbrough, RN

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators
Key Words:

Metered dose beta-adrenergic agent

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine how frequently the use of a metered dose inhaler (MDI)
bronchodilator is associated with a bronchoconstrictive response.
To investigate the nature of the response.

Technical Approach:

Routine bronchodilator responses will be measured in 500 consecutive
patients after metaproternol sulfate (MDI) in the Allergy Clinic.
A similar testing procedure will involve inhaling the inert
ingredients in the MDI by patients who demonstrated a
bronchoconstrictive response to either the albuterol MDI or
metaproternol MDI.

In the second phase it is hoped to obtain special inhalers, if
available, where one or more of the inert ingredients have been
removed and challenge the responding patients in a more selective
fashion. In patients having a bronchoconstriction to albuterol MDI
using albuterol through a turbospinhaler device will be used. In
patients having a bronchoconstrictive response to
MDI-metaproternol, an air driven in nubulizer solution will be used.

Progress:

Nine hundred patients were studied with no adverse reactions. Data
has been presented at one professional meeting and a manuscript has
been submitted for publication.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/46 Status: Terminated

Title:

An Evaluation of Possible Effects of Hepatitis Vaccine on Selected Immune Parameters

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine/Allergy C1 Assoc Investigators

Key Words:

Hepatitis vaccine

Accumulative MEDCASE
Cost

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OMA Cost:

Periodic
Review Results

Study Objective:

To determine whether the administration of hepatitis vaccine is associated with changes in selected immune functions.

Technical Approach:

Approximately 200 patients have partially or completely been immunized against Hepatitis B at our clinic. As many of these patients in the various stages of immunization as possible will be contacted and the nature of the study explained. They will be asked to donate 20 ml of blood from which the following laboratory studies will be done:

1. Hepatitis B antibody titers
2. Total immunoglobulins G, A, M, E
3. Serum protein electrophoresis
4. CBC with WBC
5. Delayed hypersensitivity skin testing to Trichophyton, Candida albicans, tetanus toxoid
6. T-lymphocytes measured by monoclonal antibody OKT3 and the subsets OKT4 and OKT5.
7. B-lymphocytes by surface immunoglobulin markers to include IgM, IgG, IgD.

These results will be compared to known normal values for these measurements which consider age and sex. If there is a suggested abnormality of any parameter, it will be pursued in a Phase II study wherein pre- and post-immunization values will be obtained in the same subject.

Progress:

Principal investigator resigned from the Army. No progress was reported. Study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/49 Status: Completed
Title:
Placental Transfer of Radiopharmaceutical and Fetal Radiation Exposure

Start Date: Est Comp Date:
Principal Investigator: Facility:
CPT M. Yedinak, DO

Dept/Sec: Dept Medicine/Nuc Med Assoc Investigators
Key Words:

Placenta: Radiopharmaceuticals

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To determine uteroplacental transfer of selected radiopharmaceuticals in an appropriate animal model (near-term pregnant sheep). The radiopharmaceuticals to be studied include Tc-99mO₄, Tc-99m RBC, Tc-99m-EHDP, and In-113mCl. A determination of fetal radiation exposure will be made. The qualitative and quantitative assessment of the radiotracer transfer will be investigated.

Technical Approach:

The placenta and fetus(es) will be externalized after appropriate anesthesia, in this case phenobarbital. The selected radiopharmaceutical will be injected, via maternal vein. An appropriate dose for the agent will be used. During this time the gamma camera will be placed over the placenta, cord, and fetus. Acquisition of the flow portion of the study will be on an A2 portable computer. Computer generated time activity curves will be created over the placentas. Static images will be obtained to qualitatively evaluate the uterus, placenta, and fetus. The length of time for static image acquisition will be determined by the agent used.

Pretreatment and sequential post-treatment serum will be obtained from the mother and fetus to quantitate the radioactivity. In addition, selected fetal and maternal organs will be obtained when the animal is sacrificed in order to quantitate the radioactivity in these organs. The organs to be studied include blood, kidney, heart, lung, liver, muscle, spleen, thyroid, testes or ovary, urine and bladder, stomach and intestines, and placenta. Sacrificing the sheep will be done with phenobarbital and T-61. Absorbed fractions for photon dosimetry will be calculated using the methods of Brownell and Loewinger. A comparison between the various determined radiation exposures to the organs of each sheep in a group will be made. A chi-square test can be performed. An analysis of variance can also be performed to compare each radiopharmaceutical group with the other.

Progress:

This study has been completed and a manuscript is in preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/51 Status: Ongoing
Title:

Biodistribution of Tc-99m-Folic Acid in 30 Normal Rabbits

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ Albert J. Moreno, MC

Dept/Sec: Dept Medicine/Nuc Med Assoc Investigators
Key Words:

Tc-99m-Folic Acid

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To radiolabel folic acid (pteroylmonoglutamic acid) with Technetium-99m and to characterize the tag using a physical description and chromatographically; to determine qualitatively and quantitatively the biodistribution of Tc-99m-folic acid in healthy rabbits.

Technical Approach:

An investigation will be conducted to determine the optimum labeling conditions for Tc-99m-folic acid. The major factors to be considered are pH. Past experience has shown that the percent of tagged material which will pass through a 0.22 u millipore filter is pH dependent. Also, folic acid appears to be labeled at either basic pH's or acidic pH's. Imaging of sheep with the apparent Tc-99m-folate demonstrated different biodistribution depending on whether the folate was labeled basic or acidic. Additionally at more physiologic pH, the Tc-99m-folate compound apparently disassociated. To isolate the tagged material at varying pH, paper chromatography will be used. The isolated material will further be characterized by U-V spectroscopy and the HPLC with the help of a chemist. The specific procedures for tagging Tc-99m as sodium pertechnetate to folic acid uses a modified stannous chloride method. After a satisfactory radiolabeled folate is achieved, biodistribution studies will be performed using a rabbit model.

Progress:

This project has not been initiated to date, but work will begin shortly.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/01 Status: Terminated

Title:

Gastric Ulcer Healing by Cimetidine, Sucralfate or Combined Therapy: Speed of Healing, Safety, and Efficacy for Ulcers Resistant to Healing by One Agent Alone.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Dennis I. Greenberg, MC

Dept/Sec: Medicine

Assoc Investigators

Key Words:

Gastric Ulcer

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To demonstrate potential synergistic effect of two drug therapy for healing of gastric ulcers. Variables to be compared include rapidity of healing, resistance to therapy (incomplete healing) and potential side-effects of single and combined therapy.

Technical Approach:

Abstract - In a 12-week double blind randomized trial, cimetidine will be compared with sucralfate and combined therapy concomitantly to assess rapidity and efficacy of medical treatment for healing of benign gastric ulcers. Any toxicity will be recorded. Untreated gastric ulcers, after a complete course of single drug therapy, will be given a four-week course of combined therapy.

Methods and materials:

a. Patient selection criteria:

(1) One-hundred-eighty patients 18 years or older will be entered into the study.

(2) Hospitalized and outpatients with one or more gastric ulcer demonstrated endoscopically between 5mm and 30mm. The largest ulcer will be evaluated if more than one gastric ulcer is present.

(3) Patients must be competent to give informed consent as per Volunteer Agreement.

b. Patient exclusion criteria:

(1) Patients unduly susceptible to cimetidine side effects (i.e. elderly, confused patients, or patients taking coumadin, aminophyllin, or dilantin that depend on hepatic P-450 cytochromal enzymes for metabolism) will be excluded. Because sucralfate is without significant systemic effects, there are no specific further exclusions.

(2) Patients with concurrent esophageal or duodenal ulcers. Prior treatment with either antacid or cimetidine longer than three days.

(3) Patients who are receiving corticosteroids, phenylbutazone, aspirin, nonsteroidal anti-inflammatory agents, or other potentially ulcerogenic drugs.

(4) Concomitant drug therapy that would include nonstudy anti-ulcer drugs, or other investigative drugs. Exceptions will be made for medications routinely used for endoscopy procedures such as atropine, diazepam, meperidine hydrochloride and simethicone; but, these will be given only on endoscopy days.

(5) Patients that have had major surgery, trauma, or burns in the preceding four weeks or during study therapy.

(6) Patients with actively bleeding ulcers.

(7) Patients with significant renal or endocrine imbalance, significance and severity to be determined by the investigator.

(8) Patients with life expectancy of less than two years.

(9) Pregnant women.

(10) Alcoholics and drug addicts.

Drugs and supplies:

(1) Sucralfate tablets, each containing 1 gm of sucralfate.

(2) Placebo tablets identical in appearance to active sucralfate test medication. The inert ingredients contained in the placebo include lactose anhydrous, Avicel pH 102 (microcrystalline cellulose), magnesium stearate and dyes.

(3) Cimetidine tablets, each containing 300 mg of active drug.

(4) Placebo tablets identical in appearance to active cimetidine test medication. The inert ingredients contained in the placebo include lactose anhydrous, Avicel pH 102, magnesium stearate and dyes.

(5) Placebo maalox T.C. (Rohrer) will be given for prn relief of pain. It will be an inert liquid compound of titanium oxide, sorbitol, etc. containing no acid neutralization capacity.

The study medication will be packaged in bottles of 68 tablets. This will supply the patient with medication for two weeks plus three days.

Patients entering the study will receive either sucralfate and placebo, cimetidine and placebo, or sucralfate plus cimetidine by random assignment.

Adverse experiences

Each adverse reaction, if encountered, will be estimated as to severity and significance. If the adverse experience is severe enough to require dropping the patient, an alternative therapy may be initiated by the investigator. Awareness of possible adverse reactions, including abnormal laboratory values, will be essential to the study.

Any patients experiencing adverse reactions, including abnormal laboratory values, shall be followed until the appropriate parameters return to baseline (normal for that patient).

Treatment plan:

Patients meeting the admission criteria will be entered into the study beginning treatment no more than 72 hours after endoscopic confirmation of duodenal ulceration and the absence of concomitant upper gastrointestinal disease. During the twelve-week period of treatment the patient will receive either sucralfate and cimetidine placebo, cimetidine and sucralfate placebo, or sucralfate and cimetidine on a double blind randomized basis. The sucralfate tablets will be swallowed with water (without chewing) one hour before the three daily meals and at bedtime. The cimetidine tablets will be taken with water (swallowed without chewing) with the sucralfate tablets one hour before meals and at bedtime. If a meal is skipped, the tablet will be taken at the time the meal would have been eaten.

Any patient showing a significant worsening of gastric ulcer disease, as judged by the investigator, will be dropped from the study and placed on alternative treatment selected by the investigator. In such cases, the circumstances and those findings leading to the decision will be fully documented in the patient's case report form and the patient will be followed until the findings return to normal or to pre-treatment levels. Such patients will be considered drug failures.

Endoscopy

Upper gastrointestinal endoscopy will be performed by an experienced staff gastroenterologist to measure the ulcer at its longest diameter with either the open tip of a biopsy forceps or an endoscopic measuring device. At least one gastric ulcer, between 5 and 30mm, but not more than three must be present without any concomitant duodenal ulcer.

Endoscopic biopsies (minimum of X4) will be required to demonstrate benignity of gastric ulcer for inclusion in this drug trial. Followup endoscopy will be scheduled for two, four and twelve weeks to allow for potentially accelerated early healing and assessment of complete healing rates. Allocation of patients to trial will be by random numbers. A double dummy technique will be used with each patient after receiving (a) cimetidine and placebo sucralfate, (b) sucralfate and placebo cimetidine, (c) cimetidine and sucralfate.

In addition, each patient will have a bottle of placebo antacid tablets and/or liquid if the above medications fail to relieve ulcer pain. The patients will be instructed to avoid the use of other antacids or anti-ulcer medication, as well as aspirin. Patients will be advised to reduce (or eliminate) smoking and alcohol intake.

These variables, as well as age, sex, occupation, coffee, family history of ulcers and gastric pH will be recorded.

Laboratory phenomenon

The following laboratory parameters will be measured at baseline and upon completion of treatment:

Hematology:

- (1) Hemoglobin
- (2) Hematocrit
- (3) RBC
- (4) WBC (total)
- (5) Neutrophils
- (6) Lymphocytes
- (7) Eosinophils
- (8) Monocytes

Blood chemistry:

- (1) Creatinine
- (2) BUN
- (3) Alkaline phosphatase
- (4) SGOT
- (5) LDH
- (6) Glucose
- (7) Cholesterol
- (8) Serum gastrin*

Urinalysis:

- (1) Specific gravity
- (2) Sugar
- (3) Protein (total)
- (4) pH
- (5) Microscopy

Stool examination:

Occult blood

*This laboratory value is required only at baseline. The investigator shall explain all laboratory values that are significantly above or below the range of normality for the particular patient in the case report form .

Informed consent and Institutional Review Board: Each patient must give written informed consent to the investigator before participating in this study (attached). In states where the legal age of consent for medical procedure is 21, patients between the ages of 18 and 21 years will have written and informed consent from a parent or guardian. A copy of the consent form will be maintained on file in the patient's permanent medical records. A copy of this protocol and the consent form used will be submitted to the Clinical Investigation Institution Institutional Review Committee for approval. A copy of the Informed Consent Approval Form is attached.

Biostatistical aspects: The critical parameter of efficacy assessment in this study is complete healing. Based on previous studies, expectation of differentiating between active treatments is not likely. Small differences between treatments with limited sample sizes may be difficult to discriminate statistically. It is usually difficult to generate adequate gastric ulcer patients in a single institution because of limited incidence.

Because of the high rate of gastric ulcer healing at 12 weeks on cimetidine therapy - 89% (NEJM J. Isenberg, 20 June 1983, p 1319-24) a multi-hospital study is desirable.

A minimum of 20 patients in each of the three study groups, for a total of 60 patients, will be the smallest acceptable number for completion of this study at William Beaumont Army Medical Center, although it is hoped that with the inclusion of other hospital groups (Thomason General and Walter Reed/other Army Medical Centers) as many as 60 patients per group (total 180) can be included within a 12 to 18 month time period.

Thus the statistical focus is to provide a statement relative to treatment equivalence. Power considerations will be addressed and confidence limits will be determined to show what differences between treatments would be required for discrimination if it actually was present. Analysis of variance or time series analyses could be used for statistics.

It is also likely that within the sample size framework discrimination between treatments for safety can be achieved.

Progress:

Principal investigator has been transferred to Fort Carson, CO, and will pursue this study at his new station.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/04 Status: Ongoing
Title:

Evaluation of the Systemic Allergic Reaction to Tetanus Toxoid

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC (Resigned)

New PI: MAJ S. Ting, MC

Dept/Sec: Assoc Investigators

Key Words:

Tetanus Toxoid

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To determine the nature of the systemic allergic reaction caused by tetanus toxoid immunization.

Technical Approach:

Using the residual serum collected from the patients, the following assays will be performed. Enzyme linked immunoassay (ELISA) determination of specific tetanus antibodies of the IgE, IgG, and IgM, IgD, subclass antibodies .

Progress:

Four patients have been entered with no adverse reactions.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/06 Status: Completed

Title:

An Investigation into Possible Antiallergic Properties of "Bee Pollen"

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

Robert W. Haverly, DAC
Lyndon E. Mansfield, MC

Dept/Sec:

Assoc Investigators

Key Words:

Bee Pollen

Accumulative MEDCASE
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OMA Cost:

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Study Objective:

To discover if there is a possible rational basis for the use of the folk medicine "Bee Pollen" in the therapy of allergic disease.

Technical Approach:

Bee pollen will be obtained from a commercial source and package in opaque capsules. Similar appearing placebo capsules will be made. Each active capsule will contain 400 mg bee pollen. The "bee pollen" will be examined for its contents and the contents noted.

Volunteers will be patients from the Allergy Clinic who have a 4+ prick skin test to Bermuda grass. They will be in good health, not pregnant, or at risk for pregnancy, and whose allergic disease can be managed without agents that interfere with skin testing. All testing will be performed when there is no natural Bermuda grass pollen exposure. All testing will be performed with extract freshly prepared from freeze-dried extracts of the same lot. All testing for each individual will be performed at the same time of day to avoid the effects of the circadian variance in skin test response.

The testing at baseline will consist of carefully performed titrated prick skin testing performed on the volunteer's back with the following reagents.

Histamine	1.0 mg/ml to .0625 mg/ml in two-fold dilutions.
Codeine	30 mg/ml to 5 mg/ml in 5 mg decrements.
Bermuda grass	1:20 W/V to 1:1280 in two-fold dilutions

The whealing and erythema responses will be transferred by a tracing technique to a permanent record. At the first visit, after the testing, the subjects will ingest 2,000 mg of bee pollen capsules, and observed for two hours to rule out the possibility of an allergic reaction to the material.

After this, they will be given a packet containing sufficient bee pollen or placebo for the following dosage schedule for a week.

Day 1	2 caps	TID
Day 2	2 caps	TID
Day 3	3 caps	TID
Day 4	3 caps	TID
Day 5	4 caps	TID
Day 6	4 caps	TID
Day 7	5 caps	TID one hour prior to retesting.

There will be four post-therapy testings. Two after a week of placebo, two after a week of bee pollen therapy. The sequence will be assigned in a randomized withdrawal fashion so that at least four patients will have two consecutive weeks of pollen capsules. The testing and measurement after each week's treatment will be the same as baseline. The testor will not know the subjects therapy regimen.

The largest wheal and erythema for each testing will be compared. The lowest concentrations which caused a 3mm wheal will be compared also.

Statistical analysis will be analysis of variance, with parametric and nonparametric methods dependent on the distribution of the data.

Each testing period after the initial challenge period will involve 45 minutes of subject/tester time.

Patients will be queried about any possible side effects.

Progress:

Twenty adults were studied with no adverse effects noted. The data was presented at a professional meeting.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/09 Status: Ongoing
Title:

Amiodarone Treatment for Severe, Refractory Cardiac Arrhythmias.

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL James H. Wilkin, MC

Dept/Sec: Cardiology Assoc Investigators
Key Words:

Cardiac Arrhythmias

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To assess long-term efficacy and adverse effects of amiodarone hydrochloride in the control of malignant, potentially malignant, or symptomatic arrhythmias in patients who are either uncontrolled by or experience limiting adverse effects to the standard available and antiarrhythmic drugs.

Technical Approach:

Amiodarone has been used as a potent anti-arrhythmic agent in Europe for many years. It does however possess several unusual properties which present problems with its utilization. The drug is a benzofuran derivative originally developed as an anti-anginal agent. The 1/2 life of this agent is very long, being in excess of 25 days. There are no reliable blood levels for monitoring the dosage of the patients. Because of these factors side effects have been chronic. It is important to have a long-term followup of patients on Amiodarone for side effects as well as efficacy. This study will provide data regarding these problems.

Progress:

One patient has been entered with no adverse reaction. This patient has been very successful in terms of arrhythmia abolition. Two other patients received the medication but received only small doses and were discontinued (not from toxic reaction).

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/10 Status: Terminated

Title:

Chemotherapy for Multiple Myeloma, Phase III (SWOG 7927/28)

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology/Hematology

Assoc Investigators

Key Words:

Myeloma

Accumulative MEDCASE

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Study Objective:

To compare the effectiveness of four different drug combinations for remission induction in previously untreated patients with multiple myeloma. Results will also be compared with those from similar therapies in recently completed Southwest Oncology Group studies.

For patients with a 75% tumor reduction; to evaluate the role of 12 months of chemotherapy maintenance with VCP or VCP plus levamisole, when compared with previous experiences.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Two patients were entered with no adverse effects to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/11 Status: Ongoing
Title:

Evaluation of Two Maintenance Regimens in the Treatment of Acute Lymphoblastic Leukemia in Adults, Phase III (SWOG 8001)

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Lymphoblastic Leukemia

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To evaluate the effectiveness, as determined by the complete remission rate of the LIO protocol using Vincristine, Prednisone and Adriamycin for induction, followed by intensive consolidation in the treatment of adult ALL in a group-wide study.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/12 Status: Ongoing
Title:

Treatment for Advanced Adenocarcinoma and Large Cell Carcinoma of the Lung: FOMi vs FOMi CAP, Phase III SWOG 8012.

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To evaluate by pairwise comparison the response-rate, duration of response and survival of 3 regimens FOMi, CAP and FOMi/CAP in patients with advanced (TMN Stage III M₁) adenocarcinoma and large cell undifferentiated carcinoma of the lung. To evaluate the degree of non-cross resistance of FOMi in CAP failures and of CAP on FOMi failures. To compare the toxicities and side effects of FOMi and CAP.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/13 Status: Ongoing
Title:

Treatment of Advanced Germ Cell Neoplasms of the Testis.

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Neoplasms

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To compare in a randomized fashion the effectiveness of the drug combination Vinblastine, Cis-diamminedichloric platinum (Cis-Platinum) and VP-16 213 versus Vinblastin Bleomycin and Cis-Platinum in the remission induction patients with disseminated germ cell neoplasms of testis origin.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Two patients have been entered into the study with no adverse reactions encountered.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/14 Status: Ongoing
Title:

A Comparison of Aggressive Radiotherapy Plus Chemotherapy Versus Aggressive Chemotherapy in the Treatment of Limited Carcinoma of the Pancreas (SWOG 8210)

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine whether aggressive therapy with combination radiotherapy/chemotherapy or chemotherapy alone yields superior survival in patients with incurable localized pancreatic cancer. To compare the toxicities of the two program.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/15 Status: Ongoing
Title:

Combined Modality Therapy for Multiple Myeloma, VMCP-VBAP for
Remission Induction Therapy.

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Multiple Myeloma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Comparison of two different methods of giving the six best
chemotherapy drugs that fight cancer.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

Three patients have been entered on this protocol. One has died,
and two are still being followed.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/17 Status: Ongoing
Title:

Use of in vitro Labeled 99mTc Red Blood Cells (RBC) Blood Pool
Imaging and Computer Aided Acquisition and Processing in
Localization of Upper Gastrointestinal (UGI) Bleeding Sites.

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Bill F. Byrd, MC

Dept/Sec: Medicine Assoc Investigators
Key Words: CPT H. Bogus
99mTc Imaging COL G. Turnbull,
Maj A.J. Moreno
LTC Tommy Brown

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the clinical utility of in vitro labeled 99mTc RBC
blood pool imaging and computer aided acquisition and processing in
the localization of UGI bleeding sites as compared to endoscopy,
contrast radiography and angiography.

Technical Approach:

Patient selection: To be included in the study, the following
criteria are necessary:

- a. The patient must be eighteen years of age, or older.
- b. The patient must give informed consent.
- c. The patient must clinically have acute upper
gastrointestinal hemorrhage manifested by a history of hematemesis
or positive gastric aspirate.
- d. Participation must be approved by the Gastroenterology
Service.
- e. All female patients age 18-45 who may be at risk for
pregnancy will have pregnancy screening test prior to procedure.

Upon admission into the study, the patient will undergo blood pool labeling per our standard technique as quickly as possible.

The patient will be imaged as soon as feasible. Feasibility will be determined by the attending physician who will consider the patient's condition and the urgency for other diagnostic or therapeutic modalities. Imaging will initially be done for 90 minutes with repeat images as necessary to document the bleeding site for up to 24 hours after labeling.

The Nuclear Medicine Service will not be apprised of the results of other diagnostic procedures, if any, until an interpretation has been recorded. The attending physician will be apprised of the Nuclear Medicine report immediately.

Data Base: The following will be collected:

Name

Age

Sex

SSN

Complete history and physical

Results of endoscopic, radiologic and surgical procedures

All serial lab data obtained on admission

Transfusion requirements

Clinical course of the patient.

Data will be collected until 30 patients have been studied. Data will be stored via the clinical chart and all computer studies will be collected and maintained on diablo disc until the study is complete.

Scintigraphic results will be compared to the other diagnostic modalities. These patients with definitive endoscopic or roentgenographic studies will be used to determine the sensitivity and specificity of the scintigraphic procedure. In those patients whose endoscopic and roentgenographic studies are inconclusive, the clinical course of the hospitalized patient will be followed and compared to scintigraphic findings.

Progress:

No patients have been entered into this study. The project will remain open.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/20 Status: Ongoing
Title:

Efficacy of Weekly Pulse Methotrexate in the Treatment of Rheumatoid Arthritis: A Double Blind Crossover Study

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ M.W. Nelson, MC

Dept/Sec: Rheumatology Assoc Investigators
Key Words:

Rheumatoid Arthritis

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

1. To evaluate the effectiveness of weekly pulse methotrexate therapy to control the activity of rheumatoid arthritis by subjective and objective criteria by means of a 27-week double blind, crossover study against placebo in patients with active rheumatoid arthritis who have failed therapy with gold salt and D-Penicillamine.
2. To evaluate the potential of long-term weekly pulse methotrexate therapy to halt or decrease the progression of destructive changes of the articular cartilage and periarticular bone by means of sequential x-ray evaluation.
3. To evaluate the potential for hepatic toxicity of weekly pulse methotrexate by sequential analysis of biochemical liver function studies (AST, ALT, alkaline phosphatase, GGT, LDH, and total bilirubin) and liver biopsy. Additionally, careful evaluation of longitudinal evaluations of hepatic morphology will allow for close monitoring of potential changes to prevent progression of methotrexate induced fibrosis to cirrhosis.

Technical Approach:

Flow sheets for laboratory parameters and clinical measurements will be maintained. Medication records will be maintained for all medications to include intra-articular medication. Laboratory

parameters and clinical measurements from week 14 and week 27 will be paired with average baseline values and analyzed using the paired t-test. If analysis does not substantiate parametric assumptions, nonparametric analyses will be substituted. Total scores for each patient will be compared for variance from baseline scores at each interval. Frequency of hepatic injury will be calculated. Comparison of clinical features, medications and dosage levels will be compared to patients without evidence of hepatic injury.

Progress:

No patients have been enrolled in this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/22 Status: Ongoing
Title:

Effect of Cromolyn on Immune Functions

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ S. Ting, MC

Dept/Sec: Assoc Investigators
CPT C.S. Serio, PhD

Key Words:

Cromolyn

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To assess the immunomodulating effects of cromolyn.

Technical Approach:

a. Animals: C57BL mice will be utilized as the animal model.

b. Dosage and Injecting Schedule: Dose levels and administration of cromolyn will be determined in preliminary experiments. We will examine a wide range of doses (all below reported toxic levels) and measure different immune functions at various times after injection to establish the time and dose kinetics.

c. Immunological measurements.

1. Lymphocyte stimulation. These assays will be utilized as an in vitro correlate of cell mediated immunity, mouse splenic, lymph node and thymic lymphocytes will be collected, separated and purified at various days after cromolyn injection (IP). T-cell responses will be analyzed by specific T-cell mitogens such as phytohemagglutinin and concanavalin A. B-cell responses will be analyzed by poke weed stimulation.

2. Antibody production. The effects of injected cromolyn on antibody production will be analyzed by using a modified plaque assay in which sheep red blood cells (SRBC) and cromolyn will be

administered interperitoneally at various times before harvesting splenic lymphocytes. Control animals will receive only SRBC.

6. STATISTICAL ANALYSIS OF THE DATA: Statistical analysis will be performed by comparing controls (non-cromolyn injected) with experimental groups using the Student's t-test.

Progress:

Abstracts of presentation of results to date:

OMOLYN (C) EFFECT ON LYMPHOBLASTOGENESIS.
Charles S. Serio, Ph.D., Stanislaus Ting, M.D.,
El Paso, Texas.

Little is known about the possible effects (C) on cell mediated immunity. We examined both in vivo and in vitro effects of (C) on lymphocyte blastogenesis in C57 Bl/6 mice. 27 animals were injected intraperitoneally (IP) with (C) or saline. Lymphocytes were tested for PHA and Con-A 7 days post-injection.

vivo Rx	PHA	
saline	73 ± 9	59 ± 1 Maximum
(C) 25 ug/kg	38 ± 1	218 ± 1 Stimulation
(C) 50 ug/kg	11 ± 2	32 ± 2 (All-cpm x10 ³ ± S.E)

x 10⁵ lymphocyte per well incubated with 1 ug/ml PHA or 1.2 ug/ml Con-A for 3 days in microtiter plates, pulsed with H³ Thymidine (16 hours and counted.) Similarly, the effects of in vitro incubation of (C) on lymphocytes from (C) and saline Rx mice was evaluated:

vivo Rx	In vitro incubation with	Con-A 0.6ug+
	0	50 ug C 25/ug C 12 ug C
saline	41 ± 2	35 ± 2 62 ± 3 108 ± 5
(C) 25 ug/kg	186 ± 8	151 ± 4 220 ± 4 225 ± 6

In conclusion it appears that in vivo (C) at certain doses (25 ug/kg) causes an increase in responsiveness of Con-A stimulated lymphocytes. PHA responses were depressed at this dose. This may represent (C) stimulation of different T lymphocyte populations. (C) or similar agents used in humans clinically may have important effects on the cellular immune system.

IN VIVO EFFECTS OF CROMOLYN ON ANTIBODY PRODUCTION. Susan McIntyre, B.S., Charles S. Serio, Ph.D., Stanislaus Ting, M.D., El Paso, Texas.

This study was undertaken to investigate whether cromolyn (C), a well-known anti-allergic agent, has any in vivo effects on antibody production.

A total of 18 C57 Bl/6 mice were divided equally into 3 groups: Group I received 0.5ml of 20% sheep red blood cell (SRBC) intraperitoneally (IP); Group II same dose (SRBC) IP plus (C) 25ug/kg IP given concomitantly; Group III (C) 25ug/kg IP 24 hours prior to (SRBC) IP. All animals were sacrificed 5 days post-SRBC injection and the number of antibody producing cells were determined by using a modified Jerne plaque assay. The results presented below represent duplicate experiments performed with triplicate samples of each splenocyte concentration used:

Cell Numbers	Group I	Group II	Group III
1 x 10 ⁶	65 ± 2	57 ± 12	283 ± 6
5 x 10 ⁵	20 ± 1	40 ± 3	308 ± 6
2.5 x 10 ⁵	5 ± 1	5 ± 1	95 ± 3

*mean plaques ± SEM

These results imply that cromolyn has immunostimulatory properties on the antibody response, which might have clinical significance and deserves further investigation.

administered intraperitoneally at various times before harvesting splenic lymphocytes. Control animals will receive only SRBC.

6. STATISTICAL ANALYSIS OF THE DATA: Statistical analysis will be performed by comparing controls (non-cromolyn injected) with experimental groups using the Student's t-test.

Progress:

Abstracts of presentation of results to date:

CROMOLYN (C) EFFECT ON LYMPHOBLASTOGENESIS.
Charles S. Serio, Ph.D., Stanislaus Ting, M.D.
El Paso, Texas.

Little is known about the possible effects of (C) on cell mediated immunity. We examined both in vivo and in vitro effects of (C) on lymphocyte blastogenesis in C57 Bl/6 mice. 27 animals were injected intraperitoneally (IP) with (C) or saline. Lymphocytes were tested for PHA and Con-A 7 days post-injection.

In vivo Rx	PHA	
IP saline	73 ± 9	59 ± 1 Maximum
IP (C) 25 ug/kg	38 ± 1	218 ± 1 Stimulation
IP (C) 50 ug/kg	11 ± 2	32 ± 2 (All-cpm x10 ³ ± S.E)

(2 x 10⁵ lymphocyte per well incubated with 10 ug/ml PHA or 1.2 ug/ml Con-A for 3 days in microtiter plates, pulsed with H³ Thymidine for 16 hours and counted.) Similarly, the effects of in vitro incubation of (C) on lymphocytes from (C) and saline Rx mice was evaluated:

In vivo Rx	In vitro incubation with Con-A 0.6ug+			
	0	50 ug C	25 ug C	12 ug C
IP saline	41 ± 2	35 ± 2	62 ± 3	108 ± 5
IP (C) 25 ug/kg	186 ± 8	151 ± 4	220 ± 4	225 ± 6

In conclusion it appears that in vivo (C) Rx at certain doses (25 ug/kg) causes an increase responsiveness of Con-A stimulated lymphocytes. PHA responses were depressed at this dose. This may represent (C) stimulation of different T lymphocyte populations. (C) or similar agents used in humans clinically may have important effects on the cellular immune system.

IN VIVO EFFECTS OF CROMOLYN ON ANTIBODY PRODUCTION. Susan McIntyre, B.S., Charles S. Serio, Ph.D., Stanislaus Ting, M.D., El Paso, Texas.

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A total of 18 C57 Bl/6 mice were divided equally into 3 groups: Group I received 0.5ml of 20% sheep red blood cell (SRBC) intraperitoneally (IP); Group II same dose (SRBC) IP plus (C) 25ug/kg IP given concomitantly; Group III (C) 25ug/kg IP 24 hours prior to (SRBC) IP. All animals were sacrificed 5 days post-SRBC injection and the number of antibody producing cells were determined by using a modified Jerne plaque assay. The results presented below represent duplicate experiments performed with triplicate samples of each splenocyte concentration used:

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2.5 x 10 ⁵	5 ± 1	5 ± 1	95 ± 3

*mean plaques ± SEM

These results imply that cromolyn has immunostimulatory properties on the antibody response, which might have clinical significance and deserves further investigation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/27 Status: Ongoing
Title:

Incidence of Mitral Valve Prolapse in Syncope

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT D.R. Wood, DO

CHANGE INVESTIGATOR TO Stephen Atchley, DO

Dept/Sec: Cardiology Assoc Investigators

Key Words:

Mitral Valve Prolapse

LTC S.T. Coleridge, DO
COL J.H. Wilkin, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine the incidence of mitral valve prolapse in patients presenting to a military Emergency Room with a chief complaint of syncope and to see if this incidence varies from a similar group of age-sex-matched controls.

Technical Approach:

The study population will consist of all patients being seen in the Emergency Room at this hospital complaining of "passing out". The patients to be studied will be ages 18-45.

A control population will consist of an age-sex-matched population presenting to the Emergency Room with either upper respiratory symptoms or acute gastrointestinal symptoms. It is anticipated that a study population of 100 subjects will be needed with 200 control subjects.

The study and control population will be obtained as follows: (a) All ER records will be screened for the complaint of "passing out". Patients meeting the criteria will be contacted by telephone. The project will be explained and if they consent, an appointment for evaluation will be set up.

If a patient presents for evaluation, two age-sex-matched controls will be selected from the ER sheets with the two diagnoses mentioned above. Studies to be obtained on all patients include a questionnaire and a m-mode echocardiogram.

Progress:

Over 100 patients have been entered into this study to date and patient entry is continuing.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/29 Status: Terminated
Title:

Treatment for Advanced Adenocarcinoma and Large Cell Carcinoma of the Lung (SWOG 8012)

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To evaluate by pairwise comparison the response-rate, duration of response and survival of three regimens FOMI, CAP and FOMi/CAP in patients with advanced (TMN Stage III M₁) adenocarcinoma and large cell undifferentiated carcinoma of the lung.

To evaluate the degree of non-cross-resistance of FOMi in CAP failures and of CAP on FOMi failures.

To compare the toxicities and side effects of FOMi and CAP.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

PROGRESS:

One patient was entered, but is now deceased.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/30 Status: Ongoing
Title:

Correlation Between Progesterone Receptor and Response to Tamoxifen
in Patients with Newly Diagnosed Metastatic Breast Disease (SWOG
8228)

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators

Key Words:

Carcinoma

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To define the prognostic role of progesterone receptor in patients
with newly diagnosed metastatic breast disease by correlating
progesterone receptor levels with objective response rates in women
treated with Tamoxifen.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/31 Status: Ongoing
 Title:

MEL 82 323 National Intergroup Protocol for Intermediate Thickness
 Melanoma 1.0 to 4.0 MM - Evaluation of Optimal Surgical Margins (2 vs
 4 cm) Around the Primary Melanoma and Evaluation of Elective Regional
 Lymph Node Dissection. (SWOG 8393)

Start Date: Est Comp Date:
 Principal Investigator: Facility:
 COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
 Key Words:

Melanoma

Accumulative MEDCASE Cost	Est OIA Cost:	Periodic Review Results
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Study Objective:

Determine the safest excision margins around the primary melanoma.
 Evaluate the management of the regional lymph nodes. Evaluate the
 relative prognostic value of various histopathological parameters of
 melanoma. The objective is to compare different histopathological
 criteria for their relative value in predicting the patient's
 clinical course and the risk of local recurrence.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
 Duplicates are kept on file in the Department of Clinical
 Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/32 Status: Ongoing
Title:

Combined Chemotherapy with Cis-Platinum, Vinblastine and
Methylglyoxal Bis (Guanyldihydrazone) (MGBG) in Epidermoid Carcinoma
of the Esophagus (SWOG 8311)

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators

Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To define the response rate and duration, as well as survival duration, in patients with advanced epidermoid carcinoma of the esophagus when treated with Cis-platinum, Vinblastine and MGBG. To determine the toxicity of this regimen in the treatment of epidermoid carcinoma of the esophagus.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/33 Status: Ongoing
Title:

Radiation Therapy in Combination with CCNU in Patients with
Incompletely Resected Gliomas of the Brain Grade I and II (SWOG 7983)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Gliomas

Accumulative MEDCASE Est Periodic
Cost OIA Cost: Review Results
Study Objective:

The major objective of this study is to compare the survival of patients with incompletely resected Grade I and II Gliomas treated with radiation alone versus radiation and CCNU. To compare the effectiveness of radiation therapy versus radiation therapy plus CCNU for remission induction and duration of remission. Because many of these patients will have poorly or nonmeasureable disease, this will only be a secondary objective.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/34 Status: Ongoing
Title:

Treatment of Limited Small Cell Lung Cancer with VP-16/Cis-Platinum,
Alternating with Vincristine/Adriamycin/Cyclophosphamide and
Radiation Therapy (SWOG 8232)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare the efficacy of alternating noncross-resistant, multidrug
regimens with concurrent combination chemotherapy as remission
induction in patients with limited small cell lung carcinoma. To
determine the toxicity of these treatment programs.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/35 Status: Ongoing
Title:

Adjuvant Chemotherapy with 5-FU, Adriamycin and Mitomycin-C (FAM) vs
Surgery Alone for Patients with Locally Advanced Gastric
Adenocarcinoma (SWOG 7804)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Adenocarcinoma

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To determine the efficacy of adjuvant chemotherapy with
5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free
interval and survival of patients with TNM stage-groups IB, IC, II
and III gastric adenocarcinoma compared to potentially curative
surgery alone.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/36 Status: Ongoing
Title:
Trial of Chlorozotocin and 5-FU in Metastatic Islet Cell Carcinoma
(SWOG 8208)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:
Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To study the response of functioning and nonfunctioning Islet Cell carcinoma chlorozotocin (CTZ) and 5-fluorouracil (5-FU). To determine the toxicity of 5-FU and CTZ when given in combination.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/37 Status: Ongoing
Title:

5-FU Adriamycin, Streptozotocin and Cyclophosphamide (FAC-S) in the Treatment of Metastatic Carcinoma Tumors

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine whether combination chemotherapy employing 5-Fluorouracil, Cyclophosphamide, Adriamycin and Streptozotocin is effective in the management of metastatic carcinoid. To study the duration of survival of patients with metastatic carcinoid tumor treated with combination chemotherapy regimens. To provide further information concerning the response and/or survival of patients with metastatic carcinoid originating in different sites and having different metastatic patterns.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/38 Status: Ongoing
Title:

Combined Modality Therapy for Breast Carcinoma (SWOG 7827)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To compare the disease-free interval and recurrence rates in estrogen receptor positive (ER+) premenopausal patients with Stage II disease, using combination chemotherapy alone versus combination chemotherapy and oophorectomy.

To compare the disease-free interval and recurrence rates in estrogen receptor positive postmenopausal patients with Stage II disease, for combination chemotherapy plus tamoxifen, tamoxifen alone, and combination chemotherapy alone.

To compare the disease-free interval and recurrence rates in all estrogen receptor negative (ER-) patients with Stage II disease using one versus two years of combination chemotherapy.

To compare the effect of these various adjunctive therapy programs upon the survival patterns of such patients.

To correlate the ER status with disease-free interval and survival.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Five patients have been entered to date with no adverse reactions encountered.

Detail Summary Sheet

Date: 1 Oct 84	Prot No: 84/39	Status: Terminated
Title:		

Speed of Healing in Acetic Acid Induced Rat Gastric Ulcers: A Comparison of Combined Therapy (Sucralfate & Cimetidine) with Single Drug Therapy (Cimetidine/Sucralfate) and no Treatment (Control Group)

Start Date:	Est Comp Date:
Principal Investigator:	Facility:

MAJ Dennis Greenberg, MC

Dept/Sec: Gastroenterology	Assoc Investigators
Key Words:	
Gastric Ulcer	MAJ Wayne O'Brien, VC Dr. Carl Pfeifer, Univ VA

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To demonstrate potential synergism for two drug therapy in the treatment of experimental rodent (rat) ulcers studied in four different groups of rats.

Technical Approach:

Experimental penetrating gastric ulcers in rats are induced by the technique described by Okabe in 1969 & 1971, Militzer in 1975, and most recently by Steiner 1982 and Fukawa 1983. Under ketamine (35 mg/kg) and xylazine (5 mg/kg) intramuscular anesthesia, laparotomy is performed through a midline epigastric incision on one hundred female Sprague-Dawley rats, weighing 225-250 grams. Glacial acetic acid (.07 ml) is topically placed on the serosal surface of the lesser curvature of the stomach (glandular region midway between the cardia and pylorus) over a mold for 60 seconds and removed with sterile gauze and normal saline. A blanching of the serosal surface indicates that an ischemic gastric ulcer will result in 24 hours. The abdominal incision is sutured and the rats are fed purina rat chow once daily between 0900 and 1100 beginning the day after operation. The rats are given p.o. (dissolved or suspended in distilled H2O) medications by lavage at 0600, 1400, 2000. There will be four equal sized groups of 25 rats. Group I is given cimetidine 80 mg/rat/tid (325 mg/kg). Group II is given sucralfate 160 mg/rat (666 mg/kg) tid. Group III is treated with cimetidine 80 mg/rat tid and sucralfate 160 mg/rat tid. Group IV is given water

tid. Rats from each group are sacrificed on days 7, 14, and 28 (by T-61 euthanasia solution). The stomachs are opened through the greater curvature. Ulcer healing is determined by observing the gastric mucosa under the dissecting microscope, grading the ulcer size and verifying by histopathology. Tissue fixed in glutaraldehyde will be studied by electron microscopy.

Progress:

Principal investigator was transferred to Fort Carson, CO, and will pursue this study at his new assignment.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/40 Status: Terminated
Title:

Cimetidine Prescription Survey in a U.S. Military Hospital in- and out-patient Population. Data from hospitalized and clinic patients compared to responses from medical staff and chart review for drug usage, efficacy, and side effects.

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ Dennis Greenberg, MC

Dept/Sec: Assoc Investigators
Key Words:

Cimetidine

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To collect data on the prescribing pattern of Army doctors for Cimetidine.

Technical Approach:

Four different surveys of cimetidine are obtained from 1) inpatients, 2) outpatients, 3) medical doctors, 4) chart reviews. One cimetidine survey will cover inpatient use while the other covers outpatients. All patients receiving cimetidine from Jan 16 to Feb 15 1984 will be given a questionnaire to voluntarily fill out. We hope to obtain enough responses in a month to determine how cimetidine is prescribed in this hospital.

A simultaneous survey for prescribing cimetidine is prepared for the medical doctors at WBAMC. The results of this questionnaire will be compared with the patients' answers to ascertain the accuracy of doctors' perceptions of disease in patients, drug compliance, general knowledge about cost of drug treatment, side effects, etc.

The first hundred charts for patients with cimetidine prescriptions in outpatient pharmacy will be checked for accuracy of recording drugs, dosages and indications for their usage by the medical staff as well as correlation with the patients statements. No attempts will be made to record personal identifying data from these charts.

The outpatient forms will be completed in the pharmacy waiting area. The inpatient forms will be distributed on the wards. We would like to gather 500 patient surveys for both groups.

The study will survey active duty military, reserve, retired dependents, etc. No attempt will be made to restrict this survey by sex, age groups, or to patients of doctors in a particular department of the hospital. The survey is meant to be broad in scope.

Progress:

Principal investigator has been transferred to Fort Carson, CO and will pursue this study at that institution.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/41 Status: Terminated

Title:

An Epidemiological Study of Peptic Ulcer Disease Among U.S. Military Patients Compared to National and International Trends

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Dennis Greenberg, MC

Dept/Sec: Medicine/Gastroenterology Assoc Investigators

Key Words:

Peptic Ulcer Disease

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine any trends (ulcer incidence vs rates for hospitalization, morbidity, and mortality) in peptic ulcer patients. To examine the effects of therapy (if any) on the natural history of ulcer disease (does cimetidine effect the need for surgery? is it cost effective?). To demonstrate the relationship of potential ulcerogenic agents (analgesic, nicotine[cigarettes], and ethanol[alcohol]) to ulcer incidence in a military population.

Technical Approach:

The peptic ulcer survey and profile will be distributed to all the patients discharged from WBAMC in 1983 with a diagnosis of either peptic ulcer, duodenal ulcer or gastric ulcer. Under 200 patients meet the criteria to enter the study and with military moves, difficulty in contacting these persons, refusal to fill out the questionnaire, deaths, etc. we hope for 50% response on this retrospective study of inpatients.

A prospective study of all patients with either a history of peptic ulcer disease in the past, or recent onset of active ulcers will be collected as these patients are seen in the Gastroenterology Clinic from January 16 to February 15 1984. If less than 100 surveys are returned, or there is insufficient data to determine if trends are statistically significant, the time period for prospective admission of patients will be extended.

Material gained will be examined for

- a. Natural history of ulcer disease
- b. Trends in peptic ulcer disease at WBAMC (compared to statistical findings from Northern Ireland hospitals) over the prior ten years.
- c. Evaluation of cimetidine for cost-benefit analysis and effect on natural history of ulcer disease.

Progress:

Principal investigator transferred and will continue this study at his new assignment. Terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/48 Status: Ongoing
Title:

The Possible Importance of Chrysosporium Tropicum as an Aeroallergen in the El Paso Area

Start Date: Est Comp Date:
Principal Investigator: Facility:
Robert W. Haverly, DAC

Dept/Sec: Assoc Investigators
Key Words LTC Lyndon E. Mansfield, MC
Chrysosporium Tropicum Gordon Roberstadt, PhD UTEP

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To ascertain if the fungus Chrysosporium Tropicum is an important allergen in the El Paso area.

Technical Approach:

Chrysosporium tropicum cultures grown on enriched media will be obtained from the mycology laboratory of GR. The hyphae and spores will be removed from the media. This material will be defatted with ether. An aqueous extract of the defatted material will be made and freeze dried. The material will be reconstituted and cold sterilized through a .22u Millipore filter. The protein concentration of the extract will be adjusted to equal the protein contents of the usual fungal allergen extracts. The final extract will be tested for sterility (fungal and bacterial) by culture technique. After sterility has been established the irritancy of two-fold dilutions of the extract will be tested in normal nonallergic volunteers chosen from investigators and staff of the Allergy/Immunology Service and the Department of Clinical Investigation.

Once a nonirritant prick puncture method concentration is established, a 50-fold dilution of this will be tested for nonirritation after intradermal injection. If this concentration is irritating, further two-fold dilutions will be made until a nonirritating dose is achieved.

Five hundred patients found allergic by skin test reaction to some allergen will be tested. Skin test negative patients to all aeroallergens will be selected also. It is estimated that between 50 to 100 such patients will be seen during the survey for 500 skin test positive patients.

The incidence of positive skin tests to Chrysosporium in the "skin test reactive" patients will be compared to the incidence of skin test reactions to Bermuda grass, Mulberry and Mesquite, Russian Thistle, and Altenaria extracts, the most common grass, trees, weeds, and mold allergens found among our patients. Special note will be made of patients, if any, who react only to Chrysosporium.

The patients who have a 3+, 4+ or 4+ ID reaction to prick skin testing will be asked to donate a 10ml blood sample for serum evaluation. If no positive reactions occur, then the second phase of the study will not be undertaken.

In Phase II, pooled sera from the responding volunteers will be used in a previously described ELISA and enzyme linked nitrocellulose immunoprint technique to characterize the nature of the antibody response to Chrysosporium Tropicum (i.e. IgE, G₁, G₂, G₃, G₄) and the proteins which are recognized as allergens.

Ten patients who have a positive skin test to Chrysosporium and a history of allergic rhinitis will be asked to return to the clinic for a nasal challenge. Briefly, the nasal challenge involves the inhalation of increasing concentrations of Chrysosporium extract into the subject's nostrils until symptoms such as sneezing, rhinorrhea, congestion, or itching occur.

Fungal extracts from Chrysosporium may be included in the routine aeroallergen testing performed at the Allergy/Immunology Service, WBAMC.

Progress:

Current evaluation of the incidence of hypersensitivity in allergic populations is underway. Difficulty has been encountered in the isolation and purification of an antigen.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/49 Status: Ongoing
Title:

A Study of the Efficacy of Pyridine Extracted Alum Adsorbed Extracts
in the Treatment of Allergic Rhinitis

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ Stanislaus Ting, MC

Dept/Sec: Medicine Assoc Investigators
Key Words: Robert Harverly, BA
Pyridine Extract

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if pyridine extracted alum precipitated allergen
extracts are suitable for allergen immunotherapy.

Technical Approach:

Forty patients, 18 years or older, will participate in this study. They will all have seasonal allergic rhinitis with a 3+ or 4+ skin test to Mesquite and Mulberry, and a clinical history which correlates with the skin tests. They will not have received immunotherapy for at least one year prior to the study. The patients will be entered into the study during the months August through October 1984.

At baseline, before beginning therapy, the following tests will be performed:

a. Carefully done titrated prick skin tests to Mulberry and Mesquite pollen with reconstituted freeze dried extracts, the same lot of which will be used for retesting late in the study. Histamine controls of 1.0mg, 0.5mg, 0.25 mg/ml and DHM controls of 1.0 ng/ml, 0.5 ng/ml, 0.025 mg/ml will be tested at the same time.

b. Nasal challenge: The patients nasal reactivity will be established by responsiveness to histamine solutions sprayed into the nose. The endpoint will be sneezing, rhinorrhea, itching or congestion. The patient will be allowed to recover and will then

have a similar challenge with Mulberry/Mesquite pollen mixture. The same endpoint determination will be used.

c. Serum will be drawn for total serum IgE, specific IgE and IgG subclass antibodies to Mulberry and Mesquite allergens.

After these tests are performed, the patients will be assigned to one of two treatment methods, aqueous extracts of Mulberry and Mesquite, or pyridine alum Mulberry and Mesquite extracts. Assignment will be selection to match groups based on the control findings.

An attempt will be made to have the patients receive 2 to 3 therapy injections weekly. During this time the patients will be carefully monitored for side reactions. When they have reached maintenance therapy, defined as 2500 PNU of each allergen per injection, and have successfully received three such injections without problems, the original baseline testing will be repeated. At this point, if other allergen immunotherapy is required for the patient's care, it will be begun and given in the alternate arm weekly, or alone during the period of increasing dosage of these other allergens. The Mulberry/Mesquite maintenance dose will be given weekly.

The study will be continued during March when the patients will fill out a daily symptom medication diary. During this time the patients in both groups will be given chlorpheniramine 4 mg tablets. A nasal decongestant (Afrin), and a topical eye preparation (OPConA) to use on a prn basis in treatment of their allergic symptoms as they occur. Daily pollen counts will be performed.

A final serum specimen for specific serum IgE, IgG subclasses to Mulberry/Mesquite will be collected. The contents of the pyridine extract, and the aqueous extract will be compared in the laboratory by isoelectric focusing and an enzyme linked immunoprint technique.

The following comparisons will be made with parametric and nonparametric statistical methods:

a. The skin titration endpoint of the reaction to the allergens, corrected for skin test reactivity as determined by histamine and DMH skin test controls.

b. The concentrations of allergen extract which cause the development of nasal symptoms at each time in the study corrected for histamine nasal reactivity.

c. The amount of total serum IgE, specific antimulberry and mesquite IgE and IgG subclass antibodies will be compared from each time specimens are collected.

d. The number and nature of side reactions, the time to reach maintenance dose of immunotherapy of each extract type will be compared (aqueous versus pyridine alum).

e. The symptom scores will be compared for each treatment group.

f. The medications use will be compared.

g. Both e. and f. will be compared to the daily pollen count.

h. The immunoprint technique will be used to denote the proteins in each extract compared to freshly extracted pollen. The number of proteins which are recognized as allergens in each extract will be compared to the fresh pollen using the pool of 40 allergic sera. The specific proteins to which the IgG subclass antibodies are formed will also be compared.

Progress:

This study has not begun because we are awaiting the extract; it should commence in the next few months.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/51 Status: Ongoing
Title:

Evaluation of Continuous Infusion Vinblastine Sulfate in Pancreatic Adenocarcinoma (SWOG 8237)

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators

Key Words:

Adenocarcinoma

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To determine the clinical response rate of a five-day continuous infusion of vinblastine sulfate in pancreatic adenocarcinoma.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/52 Status: Ongoing
Title:

Study of Doxorubicin, Mitomycin-C and 5-Fluorouracil in the Treatment of Metastatic Adenocarcinoma of the Prostate.

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Adenocarcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To test the effectiveness and toxicity of DMF (Doxorubicin, Mitomycin-C and 5-Fluorouracil) in the treatment of stage D₂ adenocarcinoma of the prostate.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/53 Status: Ongoing
Title:

Evaluation of Continuous Infusion Vinblastine in Gastric Carcinoma

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine the response rate, response duration, and duration of survival of gastric carcinoma treated with continuous infusion vinblastine. To define the qualitative and quantitative toxicities of continuous infusion vinblastine administered in a Phase II study.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients entered into the study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/54 Status: Ongoing
Title:

Immediate Post-Operative Adjuvant Chemotherapy in Patients with
Operable Breast Cancer

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Cancer

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To assess the toxicity of immediate chemotherapy with
Cyclophosphamide, Methotrexate, 5-Fluorouracil, Vincristine and
Prednisone beginning at the time of surgery in patients with Stage
II carcinoma of the breast

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

No patients entered into the study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/56 Status: Ongoing
Title:

A comparison of Zaditen with an H₁ and H₂ Antihistamine, and with a Combination of an H₁ and H₂ Antihistamine in the Inhibition of Dermographia, IND #13,303

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC L.E. Mansfield, MC (Resigned)
Change of Investigator to MAJ S. Ting, MC

Dept/Sec: Allergy/Immunology Assoc Investigators
Stanislaus Ting, MC
Ruth Hulse, LVN

Key Words:

Zaditen

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare the inhibitory effects of a new agent Zaditen with a classic H₁ antihistamine or the combination of H₁ and H₂ antihistamine.

Technical Approach:

Forty patients, 18 years or older, and practicing contraception or not capable of childbearing, will be entered into the study. They will have a dermatographic skin test response to 150g of pressure or less as determined by a special testing device. A positive response for dermatographia is defined as a 3mm or greater wheal at the scale site. For clinical purposes, absence or presence of dermatographia is important in evaluating cutaneous responses to allergen. The initial screening for reactive patients will be performed during the routine allergy skin testing performed in Allergy/Immunology Clinic, WBAMC.

After the patients understand the nature of the study, and the fact that Zaditen is an IND drug, the 40 patients will be divided into two groups. Baseline dermatographic responses will be reconfirmed and transferred by a scotch tape technique.

The medication schedule for the groups will be

GROUP A

First week	CTM 4 mg bid
Second week	CTM 4 mg qid
Third week	CTM 4 mg qid & Cimetidine 300mg qid
Fourth week	" "

GROUP B

First week	Zaditen 1 mg bid
Second week	Zaditen 1 mg qid
Third week	Zaditen 1 mg qid
Fourth week	Zaditen 1mg qid

The subjects will receive their medication as an opaque white capsule which will contain the entire dose. They will receive a new supply of medication at the second week testing. The investigator performing the dermatographia testing will be blinded to group identity of the subject. One person will perform all the testing in dermatographia. The testing will be performed at the same time of day in each person to avoid any effect of the recognized circadian rhythm of skin reactivity.

Testing for dermatographia will be performed after the first two weeks of the study, with the final testing at four weeks when the study will end.

At each testing the dermatographic response will be traced and transferred to the patient's experimental record by a cellophane technique. Three concentrations of histamine will be applied by intradermal prick skin testing (0.10, 0.05, 0.025 ng/ml) in the same area of the skin to serve as a control for skin reactivity. Similarly three concentrations of DMH (0.10, 0.05, 0.025 ng/ml) will be applied to control for mast cell mediator "releasability".

The differences, if any, between the degree of suppression of the dermatographic response by Zaditen will be compared to the H_1 and the combination for each period. The Zaditen effect, if any at two weeks, will be compared also to the four week response. A similar analysis will be performed on the histamine and DMH skin tests.

Non-parametric methods will be used for statistical analysis. The analysis will be of the least pressures which cause a 3mm wheal or greater and the lowest concentration of histamine or DMH, which cause a 3mm or greater wheal on prick puncture testing.

There will be no useage of concomitant antihistamines or systemic corticosteroids during the study period.

Zaditen and the placebo capsules will be provided by Sandoz Pharmaceuticals under IND #13,303.

Progress:

This study has not begun because investigators are still awaiting the drug.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/57 Status: Completed
Title:

Comparison of Methods for Using Metered Dose Beclomethasone Inhalers

Start Date: Est Comp Date:
Principal Investigator: Facility:

J. Yarbrough RN

Dept/Sec: Allergy/Immunology Assoc Investigators
Key Words: MAJ M.L. Smith, MSC
Beclomethasone CPT M. Hawkins, MSC
LTC L.E. Mansfield, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To compare cortisol suppression and pulmonary function in subjects using four different methods of beclomethasone inhaler treatments. The methods are (1) using an extension tube on the inhaler, (2) rinsing the mouth after inhalation, (3) using an extension tube and rinsing, and (4) using no extension tube and no rinse.

Technical Approach:

Forty-five patients currently using beclomethasone inhalers will be studied for four weeks. They will receive pulmonary function tests before and after receiving a 180 ug of inhaled albuterol (bronchodilator). Five mL of blood will be drawn between 7 and 9am for determination of serum cortisol. Subjects will measure their peak expiratory flow and record symptoms each day after arising and before retiring. After the initial battery of tests, the subjects will be put on their prescribed dose of inhaler using no extension tube and not rinsing after using their inhaler. At the end of two weeks the pulmonary function and cortisol tests will be repeated. Then subjects will be divided into age and sex-matched groups. Group A will use an extension tube or their inhaler; Group B will rinse after inhalation; Group C will use both methods for two weeks. Test will be repeated and the data analyzed by a mixed-design ANOVA.

Progress:

Twenty-one patients completed the study. Data will be presented at a forthcoming national meeting.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/59 Status: Ongoing
Title:

An Evaluation of Twice Daily Nedocromil Sodium in the Therapy of Mild to Moderate Asthma.

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Stanislaus Ting, M.C.

Dept/Sec: Allergy/Immunology Assoc Investigators
Key Words: Josephine Yarbrough RN
Nedocromil Sodium

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if nedocrimil sodium is a useful and tolerated therapy for mild to moderate asthma when given by intubation twice daily at a 4mg/ dose/

Technical Approach:

Thirty mild to moderate asthmatic patients will be selected for this study. They will be from 18 to 60 years of age, not capable of becoming pregnant, with baseline FEV₁ greater than 60%, and a 15% improvement in FEV₁ after 180 ug inhalation of albuterol, when other bronchodilators have been withheld (24 hours for theophylline, six hours for beta adrenergic agents by inhalation). They will be well controlled by routine use of bronchodilator, but will not require corticosteroid (oral or inhaled) therapy. They will be instructed in and demonstrate

1. Proper use of the meter dose inhaler.
2. The ability to properly complete the the symptoms/medication diary.

Patients who were using cromolyn or corticosteroids will have discontinued these medications for a month. Excluded will be females of childbearing potential, or who are breast feeding, patients younger than 18 years or older than 60 years, and those with any evidence of significant clinical or laboratory abnormalities.

Baseline CBC, SMA12, routine urinalysis and pulmonary functions will be obtained (Spirometry only FEV₁, FVC, FEF₂₅₋₇₅, PEFR). Each patient will participate in the study for eight weeks. The first two weeks will provide a baseline for future comparisons. At the beginning of the third week the patients will enter a six week random double blind trial, wherein many will receive either Nedocrimul 4 mg bid by inhalation or placebo. To enter this phase of the study, the patient must have demonstrated at least a total symptom score of 2 or more on 7 of the 14 days, and have demonstrated the ability to complete the symptom diary satisfactorily, and proper use of a meter dose inhaler.

Schedule of Study (Attachment #1)

VISIT #1: Entrance, entrance physical assessment examination, PFTS, Laboratory data issued diary card, issued PEFR meter to perform arising and retiring PEFR determinations. Instructed in use of MDI, PEFR meter, and how to record such data on telephone communication Seven days by monitor to evaluate progress.

Visit #2: Fourteen days: Return to Clinic, repeat PFTS, laboratory values assessed for normality, diary sheets check, 2nd instruction in use of MDI, PEFR meter with demonstration. Issued medication by Pharmacy after reassessment of suitability to enter study.

Twenty-one days: Telephone communications by monitor.

Visit #3: Twenty-eight days: Repeat of Visit #2.

Visit #4: Forty-two days: Repeat of Visit #3.
Forty-nine days: Telephone communication by number

Visit #5: Fifty-six days: End of study, repeat laboratory tests in addition to other assessments, physician assessment of overall effect of treatment on each patient.

Physician assessment.

Final Patient Assessment: 7.29 in the Fison Protocol.

Medication recording will be on symptoms diary with both OTC and prescription drugs.

Statistical analysis will compare these daily PEFR, bi-weekly spirometry) and subjective symptoms diary scores and medications use in the active and placebo groups. Changes within the group as well as difference between the groups will be evaluated using appropriate parametric and nonparametric tests for analysis.

The Pharmacy WBAMC will be responsible for maintaining the test agent in a secure location, for issuing the agents and for recording such activity in a log. Unused agents will be returned to the Pharmacy.

Severe adverse drug experience will be reported to the IRB and to Fisons within ten working days of the discovery by the investigator. Any such experience will cause the patient to be withdrawn from the study with a full written report furnished by the investigator.

Progress:

Twenty-one patients have been entered into this study with no adverse reactions. Study is ongoing.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/68 Status: Ongoing
Title:

Measurement of Plasma Histamine Levels in Nonatopic and Atopic
Individuals

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ S. Ting, MC

Dept/Sec: Assoc Investigators
Key Words:
Histamine David O. Rauls, PhD

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Using a new laboratory clinical investigation technique to establish
baseline plasma histamine levels in nonatopic and atopic individuals.

Technical Approach:

Blood drawing is a routine procedure in the Allergy Clinic for all
new patients undergoing evaluation for allergic or nonallergic
diathesis. In this proposed study, 2cc of blood will be collected
during routine venipuncture and the plasma separated for histamine
assay.

Progress: The study is proceeding very well, with 100 plasma
samples collected to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/72 Status: Ongoing
 Title:

Intergroup Phase III Protocol for the Management of Locally or Regionally Recurrent but Surgically Resectable Breast Cancer

Start Date: Est Comp Date:
 Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
 Key Words:

Cancer

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: Review Results

Study Objective:

To better define the relative roles of systemic and local treatments in the care of resectable locally or regionally recurrent cancer of the breast in patients who have no evidence of disease after resection. To assess the effects of chemotherapy, radiation therapy, singly or in combination, administered immediately after surgical resection on local control, disease-free interval, and pattern of re-recurrence. To determine the effect of the administration of systemic chemotherapy or radiation therapy which has been delayed until local, regional, re-recurrence upon local and regional control, disease-free survival, patterns of relapse and survival. To determine the influence of disease free interval, size, and extent of local or regional recurrence on the effectiveness of treatment with chemotherapy, radiation therapy, singly or in combination.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients entered into the study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/74 Status: Terminated
Title:

Diagnosis and Treatment of House Dust-Induced Asthma

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ S. Ting, MC

Dept/Sec: Allergy/Immunology Assoc Investigators
Key Words:

Asthma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine whether skin test sensitivity to house dust mite correlates with clinical symptomatology and serum specific IgE and IgG subclass to mite antigen.

Technical Approach:

Fifteen mite-sensitive volunteers, who have lived in El Paso for 2-3 consecutive years, will be asked to participate in the study. The degree of individual mite sensitivity will be determined by extinctive dilution skin test procedure. The bronchial reactivity will be first determined by Methacholine inhalation test (routine procedure in the Allergy Clinic). The bronchial sensitivity to mite allergen will be determined by mite bronchial provocation test.

Bloos will be drawn to determine mite specific IgG and IgE. House dust sampling for mite infestation will be done. Data collected from El Paso will be compared with data collected from Austin and Galveston for epidemiological study.

Progress:

Terminated. NIH grant was not received by associate investigators for a multi-center study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/82 Status: Ongoing

Title:

Combination Chemotherapy with O,P-DDD and Cis Platinum in Metastatic Adrenal Patients, Phase III(SWOG 8325)

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators

Key Words:

Chemotherapy

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To study the responsiveness of adrenocortical carcinoma to combination chemotherapy consisting of Cis-platinum (DDP) and Mitotane (O,P'-DDD). To study the prognostic features of patients with metastatic and/or resectable adrenal carcinoma receiving chemotherapy. To document the toxicity of chemotherapy in this group of patients.

Technical Approach:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/83 Status: Ongoing
Title:

Phase II Study of PAC (Cis-Platinum, Adriamycin and Cyclophosphamide)
in Treatment of Invasive Thymoma, Intergroup Study (SWOG 8490)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Thymoma

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To determine the objective response rate in extensive and limited
invasive thymoma treated with PAC (Cis-platin, Adriamycin,
Cyclophosphamide). To determine the duration of remission of patients
with limited invasive thymoma treated with split course radiotherapy
plus PAC and in patients with extensive disease treated with PAC alone.

Technical Approach:

The details are lengthy and specified in the SWOG protocol.
Duplicates are kept on file in the Department of Clinical
Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/86 Status: Ongoing
Title:

Intergroup Adult Soft Tissue Sarcoma Study #1. Randomized Trial of
Adjuvant Doxorubicin vs Standard Therapy (SWOG 8291)

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Oncology Assoc Investigators
Key Words:

Carcinoma

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

This prospective randomized study is designed to evaluate the efficacy of adjuvant Adriamycin compared to standard treatment (a delay of chemotherapy until the time of demonstrated relapse) in the management of patients with Stages IIB, IIIA-C and tissue sarcoma in terms of local recurrence rate, disease-free interval, and survival.

TECHNICAL APPROACH:

The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

No patients have been entered into this study to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/88 Status: Ongoing
Title:

SQUID Magnetocardiograph - A Pilot Study

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL James Wilkin , MC

Dept/Sec: Dept Medicine/Cardiology Assoc Investigators
Key Words:

Magnetocardiography

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the utility of SQUID magnetocardiography in the assessment of cardiovascular disease.

Technical Approach:

The SQUID magnetometer is housed in a radio frequency shielded room of the Engineering Building of UTEP. Therefore, all studies will be done at that location. It is anticipated to use six study subjects. Three will be normals, one will be left bundle branch block, one will be anterior myocardial infarction, and one will be left ventricular hypertrophy. The criteria for selecting the patients will relate primarily to the ease of obtaining the needed studies.

The subjects will receive an electrocardiogram, an echo, and a vectorcardiogram prior to the magnetocardiogram. Magnetometer will be positioned to correspond with the location of normal ECG positions.

The resultant studies will be compared. The major comparison will be in terms of the instrument's ability to define either the patient's normalacy or abnormalcy.

The technology is totally noninvasive. It does not place the patient in any kind of radio-frequency field. The other preliminary tests are noninvasive. The patients selected will have full informed consent.

Progress:

This is a newly approved study and no results have been reported to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/28 Status: Completed
Title:

Evaluation of Postpartum and Infant Care Teaching Programs at WBAMC

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ J.D. Odom, ANC

Dept/Sec: Nursing Service Assoc Investigators
Key Words:

Postpartum Care; Infant Care

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the efficacy of conducting postpartum and infant care classes for WBAMC patients.

Technical Approach:

A 30-item questionnaire has been developed from material presented to the patients in the postpartum instruction class given every Monday, Wednesday, and Friday morning on Ward 4P. This questionnaire will be administered to four groups (50 subjects in each group) who read and speak English.

Progress:

Fifty postpartum patients were included in the study with no adverse effects. The study was completed in April and the final summary report completed in August. An abstract was submitted for presentation to the Phyllis M. Verhonick Research Committee in Washington, DC in April and the paper was accepted for that competition. It will be presented at this competition on 11 September 1984. A draft for submission for publication is now in process.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/60 Status: Ongoing
Title:

Can Individualized, Detailed Preoperative Instruction Decrease
Anxiety and Enhance Recovery in the Mastectomy Patient?

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC W. Mika, ANC

Dept/Sec: Nursing Service Assoc Investigators
Key Words:

Pamela Smith, RN

Preoperative Anxiety

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

This investigation focuses on the preoperative instruction relative to the unique needs of the mastectomy patient. The goal of this research is to collect data relative to the effectiveness of preoperative instruction as perceived by the patient. This knowledge will support the hypothesis that nursing is in an ideal position to meet some of the unique needs of the mastectomy patient through preoperative instruction.

Technical Approach:

The investigator will explain to each prospective participant that each answer sheet will be coded to assure anonymity. Following collection and analysis of data, a debriefing will be arranged. Prospective subjects will be approached regarding participation regardless of military status and age. Those women who are unable to read and write English will not be asked to participate. The prospective participants will be identified by the investigator following their admission to Wards for mastectomy. Fifteen women in each group and other participants will be designated into the control group.

Progress:

Eight mastectomy patients have been entered to date with no adverse reactions or problems encountered. Interviews of patients continue.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/62 Status: Ongoing
Title:

An Assessment of Consumer Health Education Needs at William Beaumont Army Medical Center

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Jane Yaws, ANC

Dept/Sec: Nursing Service Assoc Investigators
Key Words: MAJ Betsy Kemp, ANC
Health Education MAJ Barbara Parry, ANC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To identify the perceived health education needs of consumers at William Beaumont Army Medical Center so that future patient education programs could be directed towards meeting some of these needs.

Technical Approach:

Three separate surveys will be administered by volunteers during a designated time frame. After the data has been collected it will be analyzed to examine:

1. Identify what patients perceive their health education needs to be.
2. Examine demographic data to determine if relationships exist between various items.
3. Identify what situations/methods patients identify as providing the best learning situation.

Progress:

Seventy-six adult surveys, 53 pediatric surveys, and 52 neonatal surveys were completed between June and August 1984. All of the adult surveys were administered by a Red Cross Volunteer. The neonatal and pediatric surveys were administered by the investigators. After completion of the survey forms, the data was coded and submitted to the Department of Clinical Investigation for statistical analysis. The results of the analysis have not yet been received.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/84 Status: Ongoing
Title:

Do Nurse Anesthetist's Credentials Affect Preoperative Patients Anxiety?

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT D. Gaston, ANC

Dept/Sec: Nursing Assoc Investigators
Key Words:

Anxiety

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine what effect an explanation of the Army CRNA's credentials and training will have on patient anxiety.

Technical Approach:

The sample population will be 50 ASA I adult elective preoperative patients. The patients will be given, as a pre-test, the State Trait Anxiety Inventory (STAI) test prior to pre-anesthetic interview. Twenty-five of these patients will receive added information concerning credentials and training of Army CRNA's in their pre-anesthetic interview. A repeat STAI test will be given as a post-test to assess the effect of the added information. The samples will be statistically analyzed, using the Student t-test for paired data. Demographic data will be collected for group comparison.

Progress:

This is a newly activated project. No progress has been reported.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/87 Status: Ongoing
Title:

Postpartum Nipple Care - Techniques to Prevent Sore Nipples in the New Breastfeeding Mother

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC W.V. Mika, ANC

Dept/Sec: Dept of Nursing Assoc Investigators
Key Words:
Nipple Care MAJ W.L. Farace, ANC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To evaluate the effectiveness of three different nursing approaches on the prevention of sore nipples in new breastfeeding mothers in the immediate postpartum period.

Technical Approach:

Mothers will be instructed on an individual basis by the nurse investigator on breastfeeding techniques. All mothers will be taught seven principle methods to prevent nipple pain, and two of the three experimental methods to be studied.

Mothers will be asked to fill out the subjective rating of nipple tenderness form immediately after each feeding for the first seven postpartum days. This form requires the mother to evaluate the amount of nipple pain she experienced on each breast each feeding session on a one to three scale.

Progress:

This is a newly activated study and no progress has been reported to date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 77/25 Status: Completed

Title:

A Comparison of Phospholipid Levels and Choline Phosphotransferase (CPT) Activity in Amniotic Fluid and Newborn Tracheal Fluid

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT R. Woodruff, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Phosphatidylglycerol; Amniotic fluid

COL L.L. Penney, MC
David O. Rauls, PhD, DAC

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:\$200(6111)

Review Results

Study Objective:

To determine if the level of phosphatidyl glycerol (PG) and phosphatidyl inositol (PI) or the activity of choline phosphotransferase could serve as an accurate index of lung maturity.

Technical Approach:

Amniotic fluid, and neonatal gastric and pharyngeal fluids which are normally discarded, will be analyzed for phosphatidyl glycerol, phosphatidyl inositol, choline phosphotransferase, and magnesium. The levels measured will be correlated with the incidence and severity of neonatal respiratory stress and hyaline membrane disease.

Progress:

Details of this study have been reported. The study has evolved into a clinically applicable test which may result in future publications.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/03 Status: Completed

Title:

Serial Measurement of Serum, Zinc, Magnesium, Copper, Lead, Lithium and Arsenic During Pregnancy.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL L.L. Penney, MC

Dept/Sec: Obstetrics-Gynecology

Assoc Investigators

Key Words:

Trace elements

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$417(1898)

Review Results

Study Objective:

To determine the serum levels of certain trace elements during each trimester of pregnancy in patients from the El Paso area. Specific goals will include: (1) Comparison of the serum levels of trace elements in two populations of patients, first the U.S. Army dependent population; second the native population of Thomason General Hospital. (2) To establish normal mean levels of zinc, magnesium, copper, lead, lithium, and arsenic at various stages of pregnancy. (3) To suggest future studies correlating the findings of serum levels of trace elements with pregnancy outcome.

Technical Approach:

The plan will be to determine the serum levels of copper, zinc, magnesium, lithium, lead and arsenic during the first trimester, again at 20 weeks gestation, and at term. In addition, fetal levels as determined by cord blood at delivery will be obtained. These values will be compared with nonpregnant controls.

Two separate patient populations will be compared, those of William Beaumont Army Medical Center and those of R.E. Thomason General Hospital. The two populations may reflect different levels of environmental exposure to these trace elements, as well as a possible difference in dietary intake.

a. The study would include approximately 50 pregnant patients from the OB Service, WBAMC, and a similar number of patients from the El Paso County population of RETGH.

b. Controls would be nonpregnant females of similar ages.

c. The investigation would include sampling of 10 cc vacutainer at the following intervals during pregnancy: 1st trimester, mid-trimester, time of labor and delivery, and cord blood at delivery.

d. Sampling of controls at one time.

e. A questionnaire stating the historical data pertinent to each patient will be distributed. This will request the information regarding birth place, location of residence, and employment.

f. Additional control - the studied pregnant patients will be tested at six to 12 weeks postpartum.

Progress:

Paper presented 1-3 Dec 82 at the American Chemical Society Regional Meeting, El Paso, TX. No further work with the data is anticipated.

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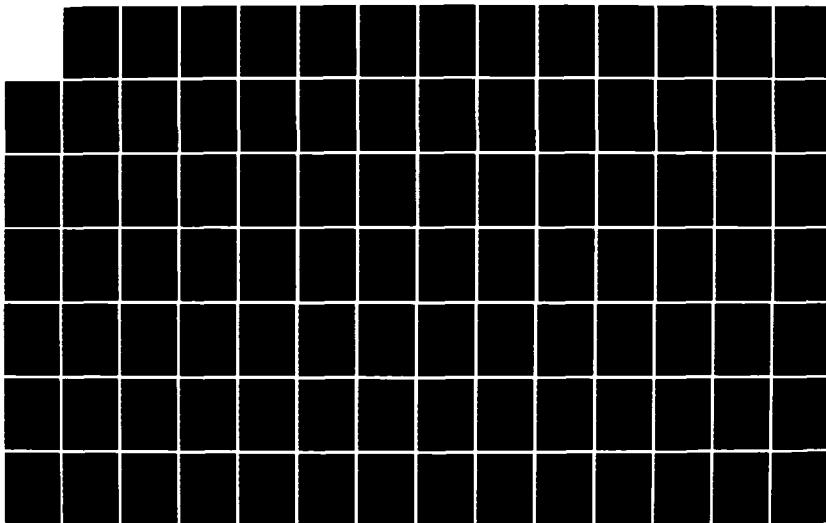
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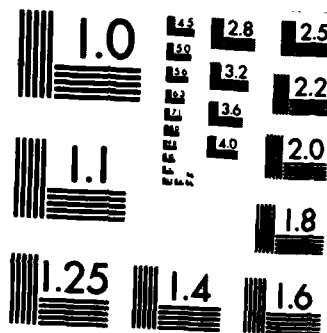
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Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/44 Status: Ongoing
Title:
Effect of Intravenous Terbutaline on Phospholipid Content of Adult Dog Lungs

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators
Key Words:

Terbutaline; Surface active phospholipids

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

This study is designed to determine if intravenously administered terbutaline will cause a change in the concentration of phospholipids known to be important in the surfactant system of adult lungs.

Technical Approach:

Two groups of 8 mixed sex adult beagle dogs each will be used in the study. One group will receive 250 ml of 0.9 percent NaCl intravenously over a 30-minute period; these will serve as controls. One-half of these animals will be sacrificed at one hour, and the other half at four hours. The other group will receive 250 ml of 0.9 percent NaCl containing 0.5 mg of terbutaline intravenously over a 30-minute period and will be similarly sacrificed. Portions of lung and alveolar washings from each animal will be freshly obtained and studied for content of total phospholipid, lecithin, sphingomyelin, phosphatidyl inositol and phosphotidyl glycerol. We will then compare the groups to determine any changes in the phospholipid content over the period of time that we investigated.

Progress:

The analysis of tracheal wash is completed, but the whole lung analyses remain. All animals have been entered and the specimens will remain frozen until personnel resources are adequate to proceed.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/46 Status: Completed
Title:

Inhibition of the Uterine Vascular Effects of 17b-Estradiol with the
H2 Receptor Antagonist Cimetidine; Cortisol; an Adrenergic Blocking
Agent, Phentolamine; and Cycloheximide

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN Assoc Investigators
Key Words:

17b Estradiol; uterine blood flow; cimetidine; cortisol;
phentolamine; cycloheximide

Accumulative MEDCASE Est Periodic
Cost OMA Cost:\$1210(1210) Review Results
Study Objective:

To quantify uterine blood flow responses two hours after a standard
stimulating dose of 17b-estradiol given IV to oophorectomized
rabbits pretreated with one of the specified agents.

Technical Approach:

The experimental model used in our previous work, Protocol 78/26,
and in a current submission for publication, "17b-Estradiol
Stimulation of Uterine Blood Flow in Oophorectomized Rabbits with
Complete Inhibition of Uterine RNA synthesis" will be used to
determine uterine blood flow with microspheres at time zero and two
hours after estradiol, 10 ug/kg IV, in animals pre-treated with
cimetidine 10 mg/kg; cortisol 20 mg/kg; phentolamine 10 mg/kg or
cycloheximide 4 mg/kg. Twelve animals will be studied in each group
and every animal will serve as its own control for comparison by
paired t-test within groups.

Progress:

Manuscript is in preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/47 Status: Ongoing
Title:

Variability of Estradiol Induced Increases in Uterine Blood Flow as a Function of Time Post-oophorectomy

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN Assoc Investigators
Key Words:

17b-estradiol; uterine blood flow

Accumulative MEDCASE Est Periodic
Cost OMA Cost: \$650(650) Review Results

Study Objective:

To establish the lack of responsiveness of uterine blood flow to estradiol stimulation in rabbits oophorectomized longer than 60 days.

Technical Approach:

We have recently completed a study of the effects of Actinomycin D on estradiol-induced increases of uterine blood flow in oophorectomized rabbits. During that experiment a delay in shipping labeled microspheres necessitated study of a small group of control animals 60 days post-operatively as opposed to between 1-5 weeks as had been the case. At 60 days an increase in uterine blood flow two hours following estradiol, 10 ug/kg, was no longer demonstrable. Such a change with time has not previously been reported. We wish to repeat the study with sufficient numbers of animals to confirm or refute this observation.

Progress:

Animals were not available in FY84 to complete this study. It is still considered worthwhile and will be completed subject to resource availability and time constraints on the principal investigator.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/48 Status: Ongoing
Title:

Variability in Quantifiable Uterine Cytosolic and Nuclear Estrogen Receptors as a Function of Time Following Oophorectomy in Rabbits

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN Assoc Investigators
Key Words:

17b-estradiol; estrogen receptors

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:0(\$618)	Review Results
Study Objective:		

To correlate the amount of receptor present with the degree of blood flow response to 17b-estradiol.

Technical Approach:

If protocol 81/47 confirms a diminished response of uterine blood flow to 17b-estradiol, as a function of time following operation, this study will be conducted. Since a decreased response is in a sense natural inhibition, a quantification for the receptors should aid in elucidating the basic mechanism. In addition to the cytosolic receptor, eosinophilic and a-adrenergic receptors, as well as any others suggested by Protocol 81/46 will be examined by standard techniques detailed in the references. For each receptor 6-8 animals will be studied at 20-40 days following operation and another 6-8 at 60-80 days.

Progress:

No work was done in FY84. The protocol is still considered worthwhile and will be pursued subject to available time from the PI.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/14 Status: Ongoing

Title:

Serum and Urinary Electrolyte and Steroid Concentrations During Danazol Administration

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN

Assoc Investigators

Key Words:

Danazol

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:\$657(647) Review Results

Study Objective:

To further define electrolyte changes occurring during danazol administration and to examine indirectly potential sites of inhibition in the metabolic pathways involved.

Technical Approach:

Standard methods of testing the mineralocorticoid pathway are available. The effects of danazol will be tested on days 6 and 12 to coincide with references in which testing was done on day 6. Our observation has been significant cramps and edema are noted 10 days to 2 weeks after starting therapy. Patients will receive 200 mg of danazol four times a day. Only those patients with documented endometriosis who will be treated as part of this therapy with danazol will be asked to participate. In addition to the battery of tests outlined in the flow chart (see below) patients will be asked to submit a serum sample at 8 a.m. for deoxycorticosterone (DOC), aldosterone (A), plasma renin activity (PRA), Na and K and to collect a 24-hour urine specimen on days 3 and 9. Aliquots of serum will be kept frozen for possible analyses of 18-hydroxycorticosterone (18OHB), corticosterone (B) or other steroids. Na, K, and possibly aldosterone will be determined on each urine collection and aliquots will be frozen for subsequent analyses (by GC-MS) as might be suggested by the serum results. Results will be collated and data analyzed by appropriate t-test after 5-6 patients have been entered to determine the need and direction of further testing.

Study Plan and Flow Chart:

- Day (-10): Subjects begin 120 mEq Na and 80 mEqK diets after 24 hour urine Na and K (Day 1 of menstrual cycle).
- Day (-5): 24-hour urine Na and K
- Day (0) :
- A) 24-hour urine Na and K completed by 0700
 - B) Baseline serum Ca, P, K, DOC, B, 18-OHB, A, PROG, 17OHP, F, DHEA and PRA.
 - C) Infusion of 25 units (0.25 mg) of ACTH intravenously at 0900. Patient supine from 0700 until 1030.
 - D) Serum drawn at 0930, 1000 and 1030 from arm opposite the infusion. All serum to be frozen and baseline and 1000 samples to be analyzed; otherwise samples to be studied if needed. Patient starts danazol. at conclusion of sampling.
- Day (6): Repeat Day (0). Patient on danazol.
- Day (12): Repeat Day (0). Patient on danazol.

Progress:

A fifth patient has now been entered and analyses are in progress.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/32 Status: Ongoing

Title:

Effect of Verapamil on Gestational Length in Rabbits

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN

Assoc Investigators

Key Words:

Verapamil

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:\$1440(1440)Review Results

Study Objective:

This is the second in a series of projects designed as preliminary studies to evaluate the potential value of verapamil as a tocolytic agent in the prevention of premature labor.

Technical Approach:

Pregnant rabbits whose time of conception is known within two hours will be used. The rabbits will be randomly divided into two groups and one group will receive oral verapamil in three equally spaced doses beginning on the 22nd day of gestation. The length of gestation will be recorded in all animals. Observations will be made regarding their respiratory status and survival of the pups. The control group will receive placebo in place of verapamil. A second cohort of rabbits will be similarly treated, but will also receive subcutaneous oxytocin 0.5 units every day at 0800, beginning on the 24th day of gestation.

Progress:

We have still been unable to satisfactorily time a shipment of pregnant rabbits. When that is accomplished, the data will be reduced and a paper prepared.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/33 Status: Ongoing

Title:

In vitro Effects of Spironolactone on Gonadotropin Production by the Rat Pituitary and Androgen Formation by the Rat Ovary

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN

Assoc Investigators

Key Words:

Spironolactone; Hormones

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$90(90)

Review Results

Study Objective:

This project is designed as a preliminary study to determine if spironolactone, acting either primarily or secondarily, inhibits gonadotropin production from the pituitary in this animal model.

Technical Approach:

Estrous rats will be sacrificed and the anterior pituitary removed for culture by established techniques. Similarly, the ovaries will be removed and separated into granulosa cell and remaining theca and stroma as published. FSH and LH will be determined by radioimmunoassay with reagents obtained from the NIH. The gonadotropins will be measured in the media of the cultured pituitary glands as a baseline and with spironolactone in concentrations of 0.15, 1.0 and 2.0 X 10⁻⁶M respectively. Glands will also be cultured in physiological concentrations of testosterone, estradiol, and estrone. Once these control levels of gonadotropin release into the media are determined, the experiment will be repeated with spironolactone combined with testosterone, estradiol and estrone individually. The effects of these same concentrations of spironolactone will also be determined on basal and gonadotropin stimulated sex steroid production from the cultured granulosa cells and ovarian stroma.

Progress:

Preliminary work and one set of studies with pituitary and ovarian cultures have been completed. Rat FSH (rFSH) and LH (rLH) radioimmunoassays have been set up and validated. Commercial

testosterone (T), estradiol (E₂), and estrone (E₁) assays have been modified for the present purposes and validated. Rapid removal techniques for pituitary and ovaries have been established and two sets of experiments with pituitary cultures have been done for 0, 0.15, 1.0 and 2.0x10⁻⁶M spiro lactone in RPMI 40 with 10% fetal calf serum. Each concentration was run in triplicate for each experiment. rLH at 18 hours culture time was 0.26-0.31 ng/100ul of culture media containing 3x10⁵ viable cells/mL. rFSH was 28.5-32.7 ng/100ul media. No differences were seen between control (0 concentration) and any of the cultures containing spironolactone.

For ovarian cultures E₂ production was 173-208 pg/ml for 2.5x10⁴ viable cells/mL. T production was lower than expected and samples are being rerun. E₁ is also being measured at this time. Similar studies for pituitary and ovarian cells stimulated with E₂ and rLH, respectively, will be done to complete the study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/38 Status: Completed

Title:

A Comparison of P.O. Vibramycin with IM Kefzol for Prophylaxis in Vaginal Hysterectomy

Start Date:

Est Comp Date:

Principal Investigators:

Facility:

CPT J.B. Stanley, MC

MAJ K. Kiley, MC

Dept/Sec: Dept Ob-Gyn

Assoc Investigators

Key Words:

Vibramycin; Kefzol; Vaginal hysterectomy

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To compare the effectiveness of an inexpensive oral antibiotic to a more expensive and painful method of prophylaxis.

Technical Approach:

Each patient to undergo vaginal hysterectomy at WBAMC will be counselled as to the need for antibiotic prophylaxis and the usual routine for administration. The study will be explained to the patient and, if not allergic to either drug, they will be asked to give written consent to join the study group. Upon entering the study group, the patient will receive two capsules at 2400 hours the night prior to surgery and an IM injection prior to going to the operating room. The study will be double blinded with all medications being distributed by the pharmacy after they have randomly selected which patients will be in each group. The two capsules taken by the patient will contain a total of 200 mg of vibramycin or a placebo. Those obtaining the vibramycin will receive an IM injection of normal saline diluted with Solu-B complex to match the color of the Kefzol solution, the next day on call from the operating room. The patient receiving the placebo capsules will receive 1 gm Kefzol IM on call from the operating room, prior to surgery. Oral vibramycin has been selected because no oral cephalosporin has ever been available and vibramycin fits all the criteria for an effective prophylactic antibiotic as set forth by Drs. Duff and Park.

The study will commence as soon as the protocol is approved and will end after 100 patients have been entered. To evaluate the study, the definition of febrile morbidity set forth by the Joint Committee on Maternal Welfare will be used: i.e., an oral temperature of 38C on two separate occasions, exclusive of the first 24 postoperative hours. Any patient developing postoperative complications would be treated with the appropriate methods, whether they are in the study group or not. Groups will be compared by X^2 analysis.

PROGRESS

Study has been completed and results will be presented at the Armed Forces District, American College of Gynecologists in Atlanta, GA, 10 October 1984. A manuscript has been submitted to Obstetrics and Gynecology for publication.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/39 Status: Terminated

Title:

Histamine Concentration in Follicular Fluid: Correlation with Follicular Size and Maturation in the Perioovulatory Period

Start Date: Est Comp Date: June 1985

Principal Investigator:
COL L.L. Penney, MC

Facility:

Dept/Sec: OB-GYN

Assoc Investigators

Key Words:

Histamine; Follicular fluid

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To obtain preliminary data regarding a possible role of endogenous histamine in ovulation.

Technical Approach:

Mature, virgin New Zealand white rabbits will be used. Follicular size will be recorded and follicular fluid histamine content measured prior to a standard IM dose of HCG and 2,4,8,12 and 16 hours following HCG in separate groups of animals. Serum estradiol and progesterone will be measured at the time of ovarian sampling in all animals.

Progress:

No further work has been possible due to time constraints on the principal investigator.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/57 Status: Ongoing

Title:
Cardiovascular Effects of Delta-9-Tetrahydrocannabinol in the
Pregnant Conscious Sheep

Start Date: 1 Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: OB-GYN Assoc Investigators

Key Words:

Delta-9-THC; Cardiovascular effects

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To delineate the effects of intravenous delta-9-THC on cardiovascular acid base parameters in the conscious pregnant sheep comparing variable doses and rates of administration.

Technical Approach:

Twelve pregnant sheep at approximately 135 days' gestation will be studied. An indwelling Swan-Ganz catheter and a carotid arterial catheter will be placed under pentobarbital anesthesia. These catheters will be maintained open with a heparin lock and the sheep will be given antibiotics. Utilizing a paired t-test and randomized block (or appropriate variance as per consultation with statistician) design the sheep will be treated 24 hours postoperatively with either 0.25 mg/kg, 0.5 mg/kg, or 1 mg/kg of delta-9-THC injected in the pulmonary artery. Baseline recordings will be obtained prior to injection and cardiac output will be monitored at 3,5,15 and 60 minutes and at hourly intervals thereafter until recovery occurs. CVP will also be monitored at the same times. Continuous monitoring of the heart rate and blood pressure will be conducted and blood gases will be drawn at 5,15 and 60 minutes and thereafter until recovery has occurred. Following rest periods of 48 hours, each sheep will be studied at the next dose in its scheme until all sheep have been studied with each of the three doses. Forty-eight hours after the final study, a continuous infusion of 10 ug/kg/min for three hours will be conducted and monitoring continued at hourly intervals until recovery occurs. The sheep will be salvaged, if possible. Serum samples will be saved at each blood gas sampling for possible analysis of THC concentration.

Progress:

A paper presentation has been accepted as attached. Further data reduction and manuscript preparation are in progress.

ACUTE CARDIO-VASCULAR EFFECTS OF DELTA-9-TETRAHYDROCANNABINOL IN CONSCIOUS PREGNANT SHEEP

L. L. Penney, A. W. O'Brien, B. E. F. Reimann, and D. O. Rauls
Departments of Clinical Investigation and Pathology, William Beaumont
Army Medical Center, El Paso, Texas 79920

The misuse of mind stimulating or sedating drugs by a large spectrum of the American population must be a matter of general concern for the physician. Among these drugs marijuana with its main active component, delta-9-tetrahydrocannabinol (Δ -9-THC) is perhaps the easiest available and has therefore received widest distribution. Although the age distribution encompasses a wide range, the young, childbearing mother is among the part of the population where regular use of marijuana is most commonly found. Therefore the question must be addressed what physiological effects of the use of Δ -9-THC can be expected. Our experiments were carried out on pregnant conscious ewes. Using a randomized design sequence three different doses of the drug, each given 48 hours apart from each other, were administered to each animal. The drug was injected into the pulmonary artery in concentrations of 0.5 or 0.25 mg/kg body weight in 5 ml ethanol within 5 minutes, or of 0.25 mg/kg body weight in 5 ml ethanol over a period of 30 minutes (8.3 μ g/kg/min). We report here the results obtained from 9 animals with the dose of 0.5 mg/kg of body weight. Four animals received the drug as dose 1, 3 as dose 2 and 2 as dose 3. The analysis of each variances indicated essentially no different responses in the parameters measured at each specified time dependent on whether the dose was administered as 1st, 2nd or 3rd in the trial. Therefore the data were pooled. The results in the ewe included a decline of the cardiac output, the mean arteial pressure, the heart rate, the total peripheral resistance, the arterial pH and of the $P_a O_2$. Elevated were the central venous pressure and the $P_a CO_2$. The implications of these findings are discussed.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/58 Status: Terminated

Title:

A Longitudinal Study of T-Cells in Pregnancy

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Steven Gardner, MC

Dept/Sec: Dept Ob-Gyn

Assoc Investigators

Key Words:

T-cells; pregnancy

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine in a longitudinal manner concentrations of helper/inducer, suppressor/cytotoxic and all peripheral t-cells during normal pregnancy.

Technical Approach:

Fifteen to twenty volunteers will be solicited from the Family Planning Clinic at the time they discontinued contraceptive measures. If an IUD or oral contraceptive was in use, baseline samples, and repeat samples at three and six week intervals, will be drawn to ascertain the stability of the controls. Those who conceive will be sampled at 6, 12, 18, 24, 30 and 36 weeks of pregnancy and again 6, 12, and 18 weeks postpartum. A single sample will be obtained during the first stage of labor. Twenty mls of heparinized blood will be removed each time so the total during pregnancy will be 140 ml. The t-cell subsets will be counted using the technique described in reference 1, with minor modifications or utilizing fluorescent activated cell sorting should that equipment be functional in our laboratory by the time the experiment is underway. Paired t-test will be used to determine significance. If possible, a cohort of nonpregnant women will be studied in a parallel manner.

Progress:

Delays in perfecting cell counting techniques prevented timely completion. Similar studies have now been published.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/07 Status: Completed

Title:

Single Dose Nitrofurantoin in Asymptomatic and Symptomatic Bacteriuria of Pregnancy

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Steven P. Gardner, MC

Dept/Sec: Dept OB/GYN

Assoc Investigators

Key Words:

Nitrofurantoin; bacteriuria

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the efficacy of a single dose of nitrofurantoin in eradicating bacteriuria of pregnancy.

Technical Approach:

Initially 200 pregnant patients with an initial routine urine culture showing greater than 50,000 colonies of a single organism per ml will be asked to participate in this study. A repeat midstream clean catch specimen of first morning void will be cultured and a positive result of at least 100,000 colonies of a single organism per ml will enable the patient to be included in the protocol. At least two cultures of greater than 100,000 colonies/ml will be required to define significant bacteriuria. A history of risk factors, i.e., prior UTIs, prior genitourinary instrumentation, sickle cell disease, diabetes mellitus and renal anomalies, will be obtained. An equal number of patients with such risk factors should be present in the study, as well as control group and the previous publication evaluating single dose therapy did not indicate increased risk, despite these factors, from the single dose therapy. A urinalysis will be done. Patients with symptomatic disease or physical or urine findings suggestive of upper urinary tract disease will be excluded. Patients with known renal parenchymal disease or creatinine clearance less than 40% will be excluded. Black patients will be advised of the potential of hemolytic anemia if they have G6PD deficiency and will be excluded if they are G6PD deficient, but they will be allowed to participate if they choose, without screening. The patient will be given either one dose of 200 mg of nitrofurantoin in the presence of the clinic

nurse or 100 mg every six hours for ten days, based on odd versus even last digit of the social security number. A repeat culture will be obtained three days later in the single dose group. Any immediate failures will be treated by an appropriate antibiotic for ten days. Followup cultures on all patients will be obtained at monthly intervals to allow identification of recurrences. An initial "cure" will be defined as negative urine cultures three days after completing either single or ten-day dosage. A more significant "cure" rate will be based on culture one month after completing either treatment duration. Cultures will be done by the calibrated loop method. The data will be analyzed by 2x2 contingency tables.

Progress:

Thirty-two cases of ABP were prospectively identified by two midstream clean catch urine specimens revealing colony counts of greater than 100,000. These patients were randomized into control and single dose (SD) treatment groups. The control group received a ten-day course of nitrofurantoin, whereas the SD group received one 200mg oral dose. Followup cultures were obtained at three days after treatment, as well as monthly for the duration of pregnancy to identify cures and to evaluate recurrences and morbidity. The control group had 16 cases with no growth at four weeks after treatment and no failures. The SD group of 16 cases had four with cure and 12 with failure. Single dose therapy may be appropriate in the nonpregnant population, but is not effective in pregnancy.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/09 Status: Terminated

Title:

Antibiotic Irrigation with Cephoxitin Solution at Cesarean Section:
Effects of Febrile Morbidity

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT G.V. Gwinn, MC

Dept/Sec: OB/GYN

Assoc Investigators

Key Words:

Cephoxitin;

**Accumulative MEDCASE
Cost**

**Est
OMA Cost:**

**Periodic
Review Results**

Study Objective:

To determine whether antibiotic irrigation with a cephoxitin solution (2 grams in 1000 cc normal saline) at the time of cesarean section, significantly decreases febrile postoperative morbidity, use of subsequent therapeutic parenteral antibiotics, severe infectious complications, and length of hospital stay.

Technical Approach:

Two hundred patients will be studied consecutively. Two groups of patients of about equal size will be compared - Group 1, Cefoxitin irrigation vs Group 2, Cefamandole irrigation. Selection will be randomized with physicians and patients blinded.

Two grams of drug will be mixed in the Operating Room with 1000cc normal saline. Patients with chorioamnionitis, intrapartum fever, anaphylactic type reaction to penicillin, or already on antibiotics will be excluded from the study. Parenteral therapeutic antibiotics will be used postoperatively whenever appropriate clinically. The two groups will be critically analyzed for similarities in percentage of patients with prolonged labor, PROM, number of vaginal exams, repeat c-section, age, race, type of skin and uterine incision, estimated blood loss, parity, and duration of operation. The charts will be reviewed shortly after discharge and analyzed for standard morbidity, positive cultures, need for therapeutic antibiotics, severe morbidity rates (wound infections, septic thrombophlebitis, etc) and length of hospital stay. Statistical analysis of the data will be performed using the chi square method.

Progress:

All investigators on this study have been transferred and no report submitted. Study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84	Prot No: 83/18	Status: Completed
Title: Inhibition of the Uterine Vascular Effects of 17-Beta Estradiol with the Beta Receptor Antagonist Propanolol and with Progesterone		
Start Date:	Est Comp Date:	
Principal Investigator: COL L.L. Penney, MC	Facility:	
Dept/Sec: OB-GYN	Assoc Investigators	
Key Words: 17-Beta Estradiol, Propanolol, Progesterone		
Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To quantify uterine blood flow responses two hours after a standard stimulating dose of 17-beta-estradiol given iv to oophorectomized rabbits pretreated with one of the specified agents.

Technical Approach:

The experimental model used in our previous work will again be utilized. Eight to twelve animals will be studied in each of three groups. The first group will be administered propanolol 0.5 mg/kg intravenously over a 5-10 minute period, beginning approximately 15 minutes prior to the baseline uterine blood flow study and administration of the 17-beta-estradiol. The second group will consist of animals administered 5 mg/kg of progesterone in 0.1 IM one day prior to the procedure, which will then consist of the standard CE¹⁴¹ baseline blood flow, administration of 10 ug/kg iv of 17-beta estradiol and a two-hour Sr⁸⁵ blood flow study. The final group will consist of animals treated with 1 mg/kg of progesterone intravenously 30 minutes prior to the remainder of the procedure. A stock solution of progesterone 1 mg/ml in propylene glycol will be utilized. One-half of the animals in the latter group will also receive a continuous infusion of progesterone from a working solution made by stirring 0.96 ml of the stock solution in 8.7 ml of 25% salt-poor albumin and diluting with 0.9% saline to a final progesterone concentration of 16 ug/ml, and infusing at .247 ml/min for the 2 1/2 hour duration of the study. Each animal will be compared at the two-hour time period to its own baseline utilizing a paired t-test. The degree of change at the two-hour time period will also be compared to control animals (already studied) by non-paired two-tailed t-tests.

PROGRESS:

These experiments are completed, but time and personnel constraints have precluded data reduction and manuscript preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/33 Status: Terminated
Title:

Effect of Breast Stimulation on Cervical Ripening

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ K. Kiley, MC

Dept/Sec: Dept OB/GYN Assoc Investigators
Key Words:

Cervical ripening

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the effect of nipple stimulation on cervical ripening in nulliparous patients at term as determined by Bishop score.

Technical Approach:

We propose to compare two groups of nulliparous, uncomplicated, term women by having one group serve as a control and the other group participate in repetitive breast stimulation until delivery and then compare cervical changes, labor and delivery, and outcome.

a. Approximately 200 subjects will be studied. These women will be delivering their first child, with an uncomplicated maternal and obstetrical history (exclusions will include advanced maternal age, hypertension, diabetes mellitus, etc.). Both active duty and civilian dependent women will be included in the study.

b. Approximately 200 controls with the same qualifications will be included.

c. Study subjects who are term by all parameters of dating (FHTs, ultrasonography, LMP) will be counselled and offered inclusion in the study. The cervix will be graded by the modified Bishop's score and the patient will be instructed in nipple rolling for 5-10 minutes with a 2-minute rest, repeating this pattern for 30 minutes four times a day. The patients will be seen weekly and the cervix re-examined. At 42 weeks estimated gestational age, nonstress testing will begin and at 43 weeks, patients will be induced for postdates. The patient will keep a record at home of nipple stimulation. Control patients will have their cervix examined and the exam recorded; they will be managed in the standard manner for postdates. The Bishop's score is a numerical rating of the cervix based on the degree of cervical dilatation, effacement and station of the presenting part.

d. Post-delivery charts will be reviewed for presenting Bishop's score, incidence of SR0M, length of labor, cesarean section rate, and fetal outcome. Comparisons will be made with the unstimulated group utilizing non-paired t-test for measurement data and chi-square testing for contingency data..

Progress:

Adverse effects have been noted by other investigators reporting on similar studies in the medical literature. The study has, therefore, been discontinued.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/44 Status: Terminated

Title:

Effect of Breast Stimulation on Cervical Ripening in the Multiparous Patient

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Kevin C. Kiley, MC

Dept/Sec: Dept OB-GYN

Assoc Investigators

Key Words:

Cervical ripening

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine the effect of nipple stimulation on cervical ripening in multiparous patients at term as determined by Bishop score.

Technical Approach:

We propose to compare two groups of multiparous uncomplicated, term women by having one group serve as a control and the other group participate in repetitive breast stimulation until delivery and then compare cervical changes, labor and delivery, and outcome.

b. Approximately 200 controls with the same qualifications will be included.

c. Study subjects who are term by all parameters of dating (FHTs, ultrasonography, LMP) will be counselled and offered inclusion in the study. The cervix will be graded by the modified Bishop's score and the patient will be instructed in nipple rolling for 5-10 minutes with a 2-minute rest, repeating this pattern for 30 minutes four times a day. The patients will be seen weekly and the cervix re-examined. At 42 weeks estimated gestational age, nonstress testing will begin and at 43 weeks, patients will be induced for postdatism. The patient will keep a record at home of nipple stimulation. Control patients will have their cervix examined and the exam recorded; they will be managed in the standard manner for postdates. The Bishop's score is a numerical rating of the cervix based on the degree of cervical dilatation, effacement and station of the presenting part.

d. Post-delivery charts will be reviewed for presenting Bishop's score, incidence of SROM, length of labor, cesarean section rate, and fetal outcome. Comparisons will be made with the unstimulated group utilizing non-paired t-test for measurement data and chi-square testing for contingency data..

Progress: Study terminated due to reports of fetal risk in uncontrolled breast stimulation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/18 Status: Completed
Title:

The Use of Medroxyprogesterone Acetate (MPA) in Decreasing Pelvic Adhesions in the New Zealand White Rabbit -a non-microsurgical model.

Start Date: Est Comp Date:
Principal Investigator: Facility:
Gwynn R. Patterson, CPT, MC

Dept/Sec: OB-GYN Assoc Investigators
CPT Pamela S. Hill, MC
COL L.L. Penney, MC
MAJ A.W. O'Brien, VC

Key Words:
Adhesions; Medroxyprogesterone Acetate (MPA)

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To evaluate whether MPA does reduce the number and severity of pelvic adhesions following crushing trauma and gross insult to the pelvic viscera of New Zealand white rabbits.

Technical Approach:

The following is the experimental outline. Twenty rabbits would undergo three surgical procedures with Rompun and ketamine anesthesia. During the first operation, the fallopian tubes would be crushed in three places bilaterally. The uterine horns would also be crushed in one place bilaterally and the peritoneum of both horns would be stripped.

Three rabbits would then undergo a second operation two weeks later. At this time lysis of adhesions would be carried out. Half of these rabbits would receive oral MPA (4 mg/kg) the day prior to the operation, the day of operation and daily for one week following operation. The other half would receive placebo in the same fashion. A third operation would then be done on all rabbits two weeks later and the rabbits would be assessed for macroscopic adhesion formation. The experiment would be carried out in a double blind, controlled fashion.

No microscopic evaluation of adhesion formation would be done as this was shown in our previous study not to be as discriminative as

macroscopic analysis. Serum MPA levels will be checked by personnel of the Dept Clinical Investigation three days after the second operation. The data will be analyzed by the one-tailed Fischer's exact test.

Progress:

The experiments are completed. Final tabulation of the observations are in progress and data reduction should be complete by the second quarter FY85.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/26 Status: Ongoing
Title:

Effects of Maternal Orgasm on Fetal Heart Rate

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Eugene Rudd, MC

Dept/Sec: OB-GYN Assoc Investigators
Key Words:

Fetal Heart Rate

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the safety (as reflected in fetal heart rate pattern) of sexual stimulation resulting in orgasm in the third trimester of pregnancy in both a normal and high risk population.

Technical Approach:

Ten to 15 patients from the routine OB Clinic will be selected for the initial phase of the testing. Patients must be low risk as defined by 1) being normotensive, 2) with appropriate fetal growth clinically, 3) single gestation and 4) with no risk factors for carbohydrate intolerance or if risk factors exist, diabetic screening must have been negative. There must also be no maternal disease to place the fetus at risk of placental insufficiency for the patient to qualify for Phase I of the study. This study is designed to determine indirectly if there is any compromise of fetal oxygenation during sexual stimulation and orgasm in a normal group of pregnant patients at 36 weeks or beyond. Following the first group of normal patients, the study will be performed using a group of patients at risk of uteroplacental insufficiency.

Progress:

Twelve normal subjects have been studied with no ill effects noted. We will recruit patients with pregnancy complications. Because of the nature of the study, recruiting volunteers has been slow.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/58 Status: Ongoing
Title:

Precision and Efficiency of Fundal Height Measurements During Pregnancy

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ E.G. Rudd, MC

Dept/Sec: OB-GYN Assoc Investigators
Key Words:

Fundal Height Measurements

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

The precision and accuracy of fundal height measurements made in a clinic consisting of multiple examiners will be evaluated in regard to documenting gestational age and uterine growth. Differences in an examiner's measuring techniques among examiners and between measurements made with and without prior knowledge of gestational age will be determined.

Technical Approach:

Patients presenting to the routine and complicated obstetrical clinics at least 16 weeks's of gestation. Gestational age will be presumed accurate when two or more of the following parameters agree: 1) reliable menstrual history, 2) first trimester exam of uterine size, 3) fetal heart tones negative to auscultation before and positive between 18-20 weeks, and 4) ultrasound dating before 26 weeks.

Progress:

Data collection has not yet begun. Starting time is anticipated in November when other projects are finished.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/75 Status: Ongoing

Title:

Efficacy of Administering a Nonsteroidal Agent Prior to
Hysterosalpingography

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Cesar Rosa, MC

Dept/Sec: Dept OB-GYN

Assoc Investigators

COL L.L. Penney, MC

Key Words:

HSG, Analgesia

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To determine whether the administration of a nonsteroidal anti-inflammatory (Ibuprofen) is effective in reducing the pain or discomfort associated with hysterosalpingography.

Technical Approach:

Patients from the Gyn Infertility Clinic, having a HSG as part of their evaluation will be invited to join the study. Ibuprofen tablets, or placebo, will be administered to the participants two to four hours prior to the HSG. Whether the patient gets the active ingredient or the placebo will be determined by the Pharmacy Svc using a table of random numbers. Medication and placebo will be of identical appearance and they will be dispensed by the Pharmacy Svc, keeping both patient and staff unaware of the nature of the medication dispensed.

Prior to the HSG each participant will be asked to complete a questionnaire that will include the following data: Age, gravity and parity, history of gynecological surgery, history of endometriosis, history of dysmenorrhea with degree and nature if any, and whether patient requires medication for dysmenorrhea.

Shortly after the procedure the participants will be asked to answer a second questionnaire. The following information will be obtained:

Was the procedure painful and , degree of pain, if any.

If painful, was pain associated mostly with the grasping of the cervix or with the injection of the contrast media.

If painful, nature of pain and for how long after the procedure did the pain last.

The day after the procedure patients will be called. The following information will be requested:

Any pain after leaving the hospital.
Was any medication necessary to relieve the pain.
Any other occurrences.

We want to determine whether administration of a nonsteroidal agent prior to hysterosalpingography helps to decrease the pain or discomfort associated with the procedure and if that was the case, whether there is any subgroup of patients that would benefit more.

Statistical Methods: Contingency tables using chi square analysis to compare placebo vs Ibuprofen; improvement or not in pain score.

The following individuals will be excluded: Patients with history of peptic ulcer disease; patients with bleeding diathesis; patients using analgesics; or patients with a history of allergy to Ibuprofen. Patients allergic to iodine, seafoods, or x-ray contrast material will be excluded.

We anticipate needing 200 individuals (100 placebo, 100 active ingredient). All patients will be referred from the Gyn Infertility Clinic. This group is composed of both active duty and dependent females in the reproductive ages of 18-40. All patients undergoing hysterosalpingography will be invited to participate except patients with the conditions previously described. The main support needed will be from the Pharmacy Svc in maintaining randomization list and codes.

The estimated duration of the study will be 1-2 years.

Progress:

This protocol has not been started yet. The placebo has been requested from Boots Pharmaceutical - manufacturers presently supplying the Ibuprofen used in our hospital. The request for placebo has been approved, the placebo should be received within the next few weeks.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/76 Status: Ongoing
Title:
Improved Pregnancy Rates after using Oil-Soluble Contrast Media
(OSCM) for Hysterosalpingography (HSG)

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ Cesar Rosa, MC

Dept/Sec: OB-GYN Assoc Investigators
COL L.L. Penney, MC

Key Words:
HSG, Pregnancy Rates, Contrast Media

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine whether OSCM used for HSG improves pregnancy rates in patients with patent fallopian tubes and no other major cause for infertility.

Technical Approach:

Patients from the Gyn Infertility Clinic will be invited to participate. After a complete initial evaluation which includes history, physical exam, semen analysis, documentation of adequate ovulatory function by BBT and serum progesterone, and postcoital test; patients will be scheduled for HSG to evaluate tubal patency as is routine in the evaluation of these infertility cases.

All HSGs will be done using water soluble contrast media (WSCM) in order to establish tubal patency and to evaluate presence or absence of rugal marks. Those individuals with a normal study as evidenced by unilateral or bilateral spillage, without evidence of distal obstruction in either tube, will then be randomized to receive 5ml of OSCM injected through the HSG cannula, or no OSCM at all. For this purpose a table of random numbers will be used assigning each group to odd or even numbers. No effort will be made to blind the study as far as the f/u will be similar in both groups and the measured parameter will be an objective, all or none end result - pregnancy.

Patients with normal studies will be followed expectantly for a minimum of four menstrual cycles during which they will be encouraged to maintain BBT charts and to time intercourse with

ovulation. After this period of time, those patients with persistent infertility will be progressed through their infertility evaluation as otherwise indicated.

Participation in this study will not change in any way the couple's infertility evaluation. The proposed waiting period after a HSG is presently the norm after any normal study; so no unnecessary or extra delay is being introduced into these patient's evaluation.

The HSG will be performed by residents from the Dept Obstetrics and Gynecology, under the direct supervision of one of the principal investigators, as is the norm for all HSGs performed presently.

Generally, whether OSCM or WSCM is used for HSG is a matter of personal choice by the operator. Both contrast media to be used WSCM (Renografin-Squiff Pharmaceuticals, Princeton NJ) and OSCM (Ethiodol-Savage Co, Missouri City, TX) have been in common use for a number of years and are accepted as safe. Patients allergic to iodine, seafoods, or x-ray contrast material will be excluded from the study.

Statistical Methods: Contingency tables, using chi-square analysis, comparing OSCM vs no OSCM; pregnancy rates in one group vs the other.

SUBJECTS: The subjects to be considered will be healthy females in their reproductive years, attending the Gyn Infertility Clinic due to involuntary infertility of more than one year duration. This group is heterogenous in terms of military status and age range 18-36.

Additional Support: Facilities to be used will be the same fluoroscopy room in the x-ray department which presently is allotted to the Gyn Dept for HSGs one afternoon a week. The maximum number of studies per day will be six, as is the norm presently. We do not anticipate the use of any additional facilities or resources other than the one routinely used for HSGs.

Progress:

Only one patient has thus far been entered. She was randomized to receive the OSCM. No untoward effects noted.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/43 Status: Ongoing
Title:

Outflow Pressure Regulation of Arthroscopic Knee Infusions.

Start Date: Est Comp Date:
Principal Investigator: Facility:
MAJ Joseph Neustein, MD

Dept/Sec: Orthopedics Assoc Investigators
Key Words:

Arthroscopic knee infusion

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

Development of an outflow pressure regulator to permit safe pressurized infusions during arthroscopy thus affording maximum visibility with minimal risk of fluid extravasation.

Technical Approach:

An experimental arthroscopy method will be developed as described below. It will be tested on a plastic hinge model knee to establish necessary parameters before being used in a controlled study.

For the controlled study patients are to be drawn from the elective surgery schedule. After informed consent they will be placed at random into a control group receiving standard treatment or an experimental group receiving treatment with the new device. Ten patients per group will be studied. Standard outflow tubing is connected to a large bore outflow portal placed in the suprapatellar pouch of the knee. This tubing is then connected in parallel and off the sterile field to #1 an air ballast, #2 a regulatory valve controlled by a pressure transducer, and #3 a manual outflow valve. A reservoir capable of delivering pressurized arthroscopic irrigation fluid (Sarns infusion pump) will be utilized. The regulatory valve on the outflow tubing will be set at 115mm of mercury, well below the minimum pressure required to rupture the knee capsule as determined by the previously quoted study. The system can be set to provide constant low flow pressure irrigation by setting the infusion pump pressure above the regulatory valve pressure. If static distension at a set pressure is desired the

infusion pump pressure will be set at or below the pressure of the regulatory valve. Quick clearing of cloudy fluid can be accomplished by opening the manual outflow valve. Both the regulatory and manual outflow valve will drain into a nonsterile collection device. The parameters measured will be the amount of time spent clearing a blurred field compared to total operating time. A Student's t-test will be used to compare control with experimental values. Complications with all procedures will be documented. No additional risks above those present during routine arthroscopy are foreseeable except the following:

1. Pressure regulation valve malfunction with failure to release pressure and subsequent extravasation of fluids through a ruptured capsule into the leg, or failure to maintain distension pressure with subsequent inadequate visualization.

Notation will be made after each case regarding any technical difficulties or advantages noted with this technique. A preliminary evaluation will be made after ten patients to determine whether continued utilization of this method is warranted.

Progress:

A prototype pressure regulator is being constructed by personnel of Medical Maintenance. When this is completed the study will proceed.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/55 Status: Ongoing
Title:

Radiolabeled Triazines for Evaluation of Soft Tissue Damage in Rabbits

Start Date: Est Comp Date:
Principal Investigator: Facility:

COL T.J. Scully, MC

Dept/Sec: Dept Orthopedics Assoc Investigators

Key Words:

COL M.J. Spicer, MC

Triazines

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Pilot study to synthesize and test a series of radiolabeled triazine compounds as nuclear imaging agents for soft tissue damage in rabbits.

Technical Approach:

Phase I: Synthesize stable complex of Indium with a chlorotriazine dye.

Phase II: Inject rabbits with radio-indium-labeled chlorotriazine dye after producing controlled soft tissue and bone lesions. Scan for radiotracer distribution within four hours.

Progress:

Phase I: A stable complex of Indium and procian brilliant blue MRS has been prepared.

Phase II: Will be initiated in the immediate future.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/63 Status: Ongoing
Title:

Comparison of Treatment Methods for Sterilization of Contaminated
Free Bone Fragments Sustained in Type III Open Fractures - An Animal
Study

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Joseph Neustein, MC

Dept/Sec: Orthopedics Assoc Investigators
Key Words:

Sterilization Bone Fragments

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Type III fractures often involve segmental loss of bone from the
wound. The following two-phase study is proposed.

Determination of susceptibility to infection of cow metatarsals
which have been contaminated by barnyard soil and then sterilized.
Determination of pullout strength of screws inserted into bone.

Technical Approach:

Stage I: Cow metatarsals will be obtained from freshly slaughtered
animals placed in plastic bags and preserved in an ice chest. The
metatarsals will be harvested and will be cut into four sections of
approximately one inch lengths. They will be incubated in barnyard
soil for 16 hours and then treated by one of the following methods.

a. Mechanical cleaning with a 10-minute betadine scrub and
sterile water.

b. Mechanical cleaning with betadine followed by autoclaving 20
minutes at 15 psi.

c. Mechanical cleaning with betadine and soaking with
merthiolate 1:1000 for one hour.

d. Controlled specimen cultured after irrigation with sterile
water.

e. Controlled culture of barnyard soil.

The specimens will be cultured by total immersion in thioglycolate broth for up to seven days with appropriate subculture for aerobic bacteria, anaerobic bacteria, and fungi.

Stage II: Four cow metatarsals will be cut into approximately two inch sections (four per metatarsal). Sections from each metatarsal will be treated by the following methods.

- a. Autoclaving for 20 minutes at 15 psi.
- b. Merthiolate 1:1000 immersion for one hour.
- c. Irrigation with sterile water for 15 minutes.

A 4.5mm ASIF cortical screw will be inserted with standard technique using a 3.2mm drill through one cortex, depth gauge determination of cortical hole, and threading the hole with a 4.5mm tap. An appropriate size screw will be inserted. An Instron machine will be used to determine pullout strength of screw from the bone. Data will be evaluated to determine if there is a statistically significant difference in results of bone treated by these various methods.

PROGRESS:

The first stage is completed. A paper is being prepared for presentation at the Society of Military Orthopaedic Surgeons in Oakland CA in November 1984.

The second stage is awaiting biomechanical pullout studies.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/85 Status: Ongoing
Title:

The Use of Gentamicin Impregnated Bone Cement in Total Hip Arthroplasty

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT P.M. Garcia, M.D.

Dept/Sec: Orthopedics Assoc Investigators
Key Words:

Arthroplasty

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the efficacy of antibiotic impregnated bone cement in total hip replacement surgery. One particular patient at WBAMC is a prime candidate for the use of this procedure and will be the only patient.

Technical Approach:

A 54-year-old diabetic male who underwent closed reduction and internal fixation of a hip fracture. Subsequently he developed osteomyelitis (Staph epi.) and was treated with six weeks of IV antibiotics and then switched to oral medication. Now clinically the infection has resolved,, but collapse of the femoral head has occurred secondary to avascular necrosis. A total hip arthroplasty will be placed with the use of antibiotic impregnated cement. Use of antibiotic impregnated cement for total joint arthroplasty following infections is highly recommended on a protocol from EM Laboratories.

Progress:

Newly activated. No progress to report at this date.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/60 Status: Ongoing

Title:

Interactions Between Aminoglycoside Antibiotics and Vitamin B6 in vitro and in vivo

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ R.C. Keniston, MC

Dept/Sec: Dept Pathology

Assoc Investigators

Key Words:

Aminoglycosides; Vitamin B₆

**Accumulative MEDCASE
Cost**

**Est
OMA Cost:**

**Periodic
Review Results**

Study Objective:

To develop a method for isolating and quantitating aminoglycosidepyridoxal-5'-phosphate complexes. To isolate these complexes from the urine of patients receiving the aminoglycoside antibiotics. To determine if depletion of vitamin B6 occurs in patients receiving aminoglycoside antibiotics, and if so, how this depletion correlates with morbidity and mortality.

Technical Approach:

Subjects will be patients who are to be given aminoglycoside antibiotics for clinical indications (sepsis, serious gram-negative infections, etc). These patients should also have SMAC 20 chemistry screens and monitoring of their aminoglycoside levels (procedures already routinely performed). The blood and urine samples from at least 30 patients will be examined.

Progress:

Few patients have been eligible, consequently no patients have been entered. The study is ongoing.

Detail Summary Sheet

Date: 1 Oct 84 Prot No:83/34 Status: Ongoing
Title:

Utilization of Robotics in the Laboratory

Start Date: Est Comp Date:
Principal Investigator: Facility:
CPT P.H. Cordes, MC

Dept/Sec: Dept Pathology Assoc Investigators
Key Words:

Robotics

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To investigate the uses of a simple robot in application to menial and repetitive tasks within the laboratory. To determine whether such applications might be cost effective. To determine what other applications might be feasible and cost effective in the laboratory with more sophisticated robots.

Technical Approach:

- a. Purchase robot.
- b. Build robot (time frame 1-2 weeks).
- c. Begin investigation.

(1) Develop application to routine histological staining. A routine and repetitive task requiring only simple programming sufficient for familiarization with the machine (time frame 2-3 weeks).

(2) Develop application to production of microbiological media. A routine and repetitive task requiring more detailed manipulation of the robot arm and more than one program in order to deal with more than one media type (time frame 1-2 months).

(3) Develop and test application for delivery of laboratory specimens from receipt to the appropriate section. A routine task requiring intensive programming in robot navigation, obstacle avoidance, motion detection and voice output (time frame 3-6 months).

(4) Implement other possible uses that become apparent during utilization of the robot, but which are unforeseen at this time.

d. Evaluation.

(1) Reliability: The ability of the robot to perform a task more than once without reprogramming. Also an estimation of mean time between failures of the hardware.

(2) Suitability: Is this particular robot suitable for this job and/or environment? Would a more sophisticated robot be suitable?

(3) Cost effectiveness: Is the robot cost-effective in each of the above implementations? Would a more sophisticated robot be cost effective?

e. Reporting of results: Writing of an article for publication and/or presentation to laboratorians at a conference.

Progress:

The robot has been purchased and constructed, however difficulty has been encountered and the robot is in the process of repair.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/66 Status: Completed
Title:

Effect of Pyridoxal-5'-Phosphate on Polyamine and Gentamicin
Toxicity in Rats

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ R.C. Keniston, MC

Dept/Sec: Pathology Assoc Investigators
Key Words:

Toxicity

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To see if pyridoxal-5'-phosphate can prevent or ameliorate the renal, hepatic, and pulmonary toxicity of the polyamines and gentamicin.

Technical Approach:

Sprague-Dawley rats, 250-300gm each will be the model for this study. Group 1 will be saline-saline controls; Group 2 will be saline-PLP controls; Group 3 will be SPM-saline or GM-saline controls. Group 3 should die of renal failure in 4-10 days.

Progress:

PLP appears to be an effective antidote for poisoning by SPM, GM, and KCN. The vitamin prevents seizures and acute death from respiratory paralysis and also prevents acute tubular necrosis and death from renal failure. The amine-PLP and cyanide-PLP complexes appear to be nontoxic, and these complexes apparently form rapidly in the body, as they do in vitro. Apparently it is critical to have at least a molar equivalency of PLP to the toxic substance to prevent the acute toxic effects. PLP appears to have no significant acute or chronic toxicities, and even appears to stimulate growth, renal and lymphoid function.

A paper is in preparation detailing results of this study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/42 Status: Completed

Title:

The Recognition and Frequency of the Polycystic Ovary Syndrome in a General Adolescent Population

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT W.R. LaForce, MC

Dept/Sec: Pediatrics

Assoc Investigators

Key Words:

Polycystic ovary syndrome

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost: \$0(2852)

Review Results

Study Objective:

To establish the frequency of biochemically proven polycystic ovary syndrome (PCOS) in a general adolescent clinic population, and to evaluate parameters of the medical history in its early recognition.

Technical Approach:

Each year in May through August days are set aside for school and sports physical examinations for dependent children at WBAMC. Approximately 350 adolescent girls are examined on these days. Sera will be collected from approximately 200 of these adolescents after patient and parental consent, and a menstrual history will be obtained. Serologic RIA tests will include the gonadotropins LH and FSH, and the androgen testosterone. Aliquots of serum will be kept frozen for possible subsequent hormone analysis to include estrone, estradiol, androstenedione and insulin. Elevated levels of testosterone, and/or elevated LH, with associated low values of FSH, are biochemical evidence of the polycystic ovary syndrome. Patients characterized as cases of this syndrome will be asked to return to the Adolescent Medicine Clinic for further evaluation, including more comprehensive medical history, and pelvic examination. Those cases identified will be counselled regarding future fertility problems, and offered biochemical regulation of their menstrual periods in an effort to offset the symptoms of this disorder.

Progress:

Data was collected from 283 girls. Age, age at menarche, menstrual age, frequency of period, height, weight, use of birth control pills and clinical observation were determined for each girl. Serum progesterone, FSH, LH, testosterone, and free testosterone were measured. Data analysis is underway.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/66 Status: Terminated
Title: Single Day Therapy with Trimethoprim-Sulfamethoxalate for
Lower Urinary Tract Infection

Start Date: _____ Est Comp Date: _____
Principal Investigator: _____ Facility: _____

LTC R. Lampe, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Urinary tract infection

Accumulative MEDCASE Cost	Est OHA Cost:	Periodic Review Results
Study Objective:		

To determine if a single day of therapy is just as effective as ten days of therapy for lower urinary tract infection. Single day therapy would cut cost, potential development of resistant organisms would be reduced, and patient compliance would be increased.

Technical Approach:

Fifty children, ages 2-12 years will be studied. Children who would not be included: (1) Antibiotic therapy within previous 48 hours. (2) Diabetics. (3) Known anatomic or vascular abnormality of the kidney, or impaired renal function. (4) Any indication of upper urinary tract infection, i.e. flank pain, vomiting, fever greater than 38°C. (5) Known allergy to sulfa drugs.

The diagnosis of lower urinary tract infection will be based upon a) lower abdominal pain, b) frequency of urination, c) urgency or urination, d) dysuria, e) no fever, or fever less than 38°C, f) no flank pain or tenderness, g) child does not appear ill (toxic).

Laboratory: One or more of the following: a) unspun urine with bacteria but no casts. b) dipstick-nitrite positive. c) greater than 100,000 colonies on two clean catch urines. d) greater than 10,000-50,000 colonies on a catheterized specimen. e) any growth on a suprapubic aspiration of the bladder.

A complete blood count, ESR, and C-reactive protein will be drawn on all subjects in the study. Selection for single day vs. ten day therapy will be random. Fifty envelopes, twenty-five of which will contain the single day protocol, and twenty-five of which will contain the ten-day protocol, will be utilized for the selection.

The subjects of the study will receive 8 mg per kilogram body weight per dose of trimethoprim-sulfamethoxazole. They will receive one dose at the time they are seen in the clinic and one dose at bedtime that same day. The controls will receive 4 mg per kilogram body weight per dose of trimethoprim-sulfamethoxazole every twelve hours for a period of ten days.

Each child included in the study will be seen 48 hours after institution of therapy at which time a repeat urine microscopic, dipstick, and culture will be done. At that time children who will be excluded are: (1) initial negative urine culture (2) organism not sensitive to trimethoprim-sulfamethoxazole. (3) Any child who shows signs or symptoms of upper urinary tract infection.

Subsequent to the initial 48 hour followup each patient will be seen two weeks after initiation of therapy, then monthly for six months. All male children will also be studied for urinary tract abnormalities with an intravenous pyelogram and a voiding cystourethrogram.

Progress:

Principal investigators are unable to enroll and follow patients due to patient care and administrative responsibilities. Results (preliminary) indicated that single day therapy was not adequate, so no further patients were enrolled. A total of ten patients were enrolled with no adverse effects reported.

SINGLE DAY VS. TEN-DAY TREATMENT OF URINARY INFECTIONS IN CHILDREN USING TRIMETHOPRIM-SULFAMETHOXAZOLE. W.E. Egerton*, A.M. Muelenaer*, M.R. Weir, R.M. Lampe, William Beaumont Army Medical Center, El Paso, TX.

Single dose treatment of urinary tract infections in adults can be an effective alternative to traditional ten-day therapy with antibiotics. Cure rates of 50% to 85% with single day treatments have been cited in comparison to cure rates of 65% to 85% with ten-day treatments. To test this hypothesis, children between ages 2 to 12 with one or more of the following signs: (a) lower abdominal pain (b) urinary frequency (c) urinary urgency (d) dysuria (e) no fever or fever less than 38 Centigrade (f) no flank pain (g) non-toxic appearance were studied and randomly assigned single day trimethoprim/sulfamethoxazole (TMP-SMX) or TMP-SMX twice daily for 10 days. Laboratory confirmation was based on one or more of the following: (a) unspun urine with bacteria but no casts (b) dipstick-nitrite positive (c) greater than 100,000 colonies on two clean catch urines (d) greater than 10,000 to 50,000 colonies on a catheterized specimen or (e) any growth on suprapubic aspiration of the bladder. Each child was seen 48 hours after initiation of therapy and a culture obtained. At that time children with organisms resistant to TMP-SMX, negative initial cultures or the development of upper tract signs were excluded. Cultures were also taken at two weeks after institution of therapy. Erythrocyte sedimentation rate and C-reactive protein were obtained when possible. Thirteen patients have met the criteria for entry and have completed follow-up. Each of the nine patients receiving 10 days of TMP-SMX had sterile urine 48 hours after initiation of therapy and eight of nine patients had sterile urine two weeks after conclusion of therapy. Each of four patients receiving TMP-SMX for one day had sterile urine 48 hours after initiation of therapy; however, three of four patients had significant bacteriuria two weeks after conclusion of therapy. Seven patients had erythrocyte sedimentation rates obtained and all were less than 20 mm per hour. Four of eight patients had positive C-reactive protein in the serum. Three of these four had bacteriuria two weeks after the conclusion of therapy. (Two were in the single day therapy group and one was in the ten day therapy group.) These preliminary results suggest that single day treatment may not be as satisfactory as ten days TMP-SMX for urinary tract infection.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/09 Status: Ongoing

Title:

An Evaluation of the Effects of Theophylline and Beta Adrenergic Medication on the Auditory Processing Ability of Children

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT G.V. Gwinn, MC

CHANGE INVESTIGATOR TO MAJ A.W. Atkinson, MC

Dept/Sec: Dept Pediatrics

Assoc Investigators

Key Words:

Theophylline

**Accumulative MEDCASE
Cost**

**Est
OMA Cost:**

**Periodic
Review Results**

Study Objective:

To determine if the use of theophylline or beta adrenergic medications qualitatively or quantitatively affect the auditory processing abilities of children.

Technical Approach:

Twenty asthmatic children currently requiring continuous therapy with theophylline will be entered into the study. Serum theophylline levels will be checked to ensure that they are in the generally accepted therapeutic range of 10-20 micrograms per milliliter.

Each child will be evaluated using the Revised Token Test administered by personnel from the University of Texas at El Paso Speech, Hearing and Language Center. The reliability in the administration of this test is verified to be greater than 98%. The testers will be unaware of which medical regimen the children are on during any of the testing encounters.

Patients will then have their theophylline therapy discontinued and be placed on an inhaled beta-2 agent (Albuterol 180 micrograms) four times daily. Clinical experience suggests that most patients do equally well on this regimen. After one week on this new regimen, the testing will be repeated.

Patients whose clinical condition suggests that their asthma would be adequately controlled on inhaled beta-2 medication taken on an as needed basis will be placed on Albuterol every four to six hours as needed. After one week, they will be retested.

During the fourth week, the subjects will have the inhaled bronchodilators discontinued and once again be placed on their

theophylline regimen. After one week they will be tested once again.

The patient's pulmonary condition will be monitored by a diary sheet and twice daily Peak Expiratory Flow Rates. Conventional spirometry and flow volume determinations will be determined weekly.

After the results are analyzed each child will be placed on the regimen which gave best control of asthma and the least CNS effects.

The theophylline preparations used in this study will be whichever preparation the patient is taking on initiation of the study.

Statistical analysis will be done with nonparametric and parametric testing as deemed proper by our statistical consultant.

Progress:

Dr. Gwinn has been transferred and a new investigator, MAJ A.W. Atkinson, MC, will pursue this study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/43 Status: Ongoing

Title:

Adolescent Immunity to Varicella and Cytomegalovirus

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC M. Schydlower, MC

Dept/Sec: Dept Pediatrics

Assoc Investigators

Key Words:

Varicella; Cytomegalovirus

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the immune status of adolescents age 13-17 years to varicella and cytomegalovirus.

Technical Approach:

Each year, May through August, days are set aside at WBAMC for school and sport physical examinations for military dependent children and adolescents as required by the local schools. Approximately 300 adolescents are examined on these days. Sera will be collected from approximately 150 adolescents and analyzed for seronegativity for varicella by complement fixation and neutralization tests. Sera will also be tested for cytomegalovirus by complement fixation and anticomplement immunofluorescence. The laboratory of Dr. Philip Brunell at the Department of Pediatrics, University of Texas Health Science Center, San Antonio, will test for varicella, and the laboratory of Dr. Martha Yow, Department of Pediatrics, Baylor University in Houston, will test for CMV. Both are experts in the study of these viruses. The data obtained will be correlated with age, sex, ethnic background, rank (as an index of economic background) and history of disease. Approximately 5 cc of blood will be obtained by venipuncture after obtaining appropriate informed consent.

Progress:

Varicella portion has been published in the New England J Medicine 311:329, 1984. CMV portion: Data is already being evaluated in preparation for a presentation and/or publication. A total of 107 adolescents (mean age 15.9 years) have been entered with no adverse effects.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/45 Status: Terminated

Title:

Use of VM-26 in Acute Leukemia

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

Jerry J. Swaney, M.D., DAC

Dept/Sec: Dept Pediatrics

Assoc Investigators

Key Words:

VM-26; Leukemia

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

VM-26 will be used as remission induction agent and maintenance agent for refractory acute leukemia in children and adolescents. The response rate to VM-26 will be evaluated, as well as its toxicity.

Technical Approach:

Patients to be enrolled for this evaluation will be those children or adolescents with acute leukemia in relapse and refractory to other available chemotherapeutic agents. The number to be enrolled is unknown as this will vary with number of children and adolescents who relapse.

Attempts at induction of remission in refractory acute leukemia in bone marrow relapse will be undertaken with combination chemotherapy of intravenously administered VM-26 and cytosine arabinoside. After determination of hematologic relapse and evaluation of renal and hepatic function with standard laboratory tests chemotherapy will be instituted.

The patients will have prior to beginning therapy a bone marrow aspiration and biopsy, spinal tap, SMA 20, and CBC with platelets. A hemogram will be obtained prior to every course of therapy and an SMA-20 prior to every other course.

Intravenous chemotherapy will be semi-weekly for a total of eight courses. These will be administered on a Monday and Thursday or a Tuesday and Friday schedule for four consecutive weeks. A bone marrow aspiration will be done preceeding the first and fifth courses, and at the time a ninth course would be due.

CHEMOTHERAPY PLAN:

VM-26 will be given in combination with cytosine Arabinoside (Ara-C, Cytosar) for induction and maintenance therapy.

VM-26 165 mg/m² IV 2 times a week for 4 infusions and cytosine Arabinoside 300 mg/m² IV just prior to VM-26 2 times a week for four injections. The VM-26 will be mixed at 1 mg/cc in .05 D 1/3 NS to be infused over 30-60 minutes. The Ara-C will be mixed as per package instructions and given IV push.

Bone marrow aspiration and biopsy will be performed Day 15 to determine marrow status and cellularity. Evaluation of peripheral demogram, bone marrow status and patient status will determine if the chemotherapy is to be continued, or modified. Maintenance therapy will consist of the above regimen given every two weeks.

Data will be recorded on the hematology flow sheets currently in use. Copy of consent will be maintained in folder.

Progress:

The principal investigator was never included on the IND at the National Cancer Institute. Study is terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/23 Status: Terminated
Title:
Cytomegalovirus Antibody and Serioconversion Among Hospital Personnel

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL R.M. Lampe, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Cytomegalovirus

Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
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Study Objective:

To determine serologic immunity to cytomegalovirus among hospital personnel and the frequency of seroconversion during a nine-month period.

Technical Approach:

Subjects for the study will be hospital personnel who volunteer have sera drawn initially and nine months later.

Procedure: Period I: Serum drawn from each subject will be stored at -20° in a labeled tube sent from NINCDS, and a form prepared for each subject.

Period II: Nine months later a second serum specimen will be drawn and the form completed. Paired serum specimens will be sent to NINCDS for CMV antibody assay together with the forms. Antibody assays to be performed by ELISA and/or indirect hemagglutination.

Progress:

This study will not be completed as a similar study has appeared in the medical literature.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/26 Status: Terminated
 Title:
 The Efficacy of Oral Electrolyte Solution in Acute Gastroenteritis
 in Pediatric Inpatients at WBAMC

Start Date: Est Comp Date:
 Principal Investigator: Facility:
 CPT Mark Crowe, MC

Dept/Sec: Dept Pediatrics Assoc Investigators
 Key Words:

Gastroenteritis

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: Review Results
 Study Objective:

To acquire information and experience in treatent with the World Health Organization's Oral Rehydration Solution in children with acute gastroenteritis and associated dehydration.

Technical Approach:

a. Purpose: To acquire information and experience in treatment with the World Health Organizations - Oral Rehydration Solution in children with acute gastroenteritis and associated dehydration who are admitted to William Beaumont Army Medical Center. This data would be valuable in supporting or refuting other similar studies conducted in this area.

b. Subjects: A minimum of sixty children, age three months to four years of age, who are admitted with a diagnosis of dehydration secondary to diarrhea of less than seven days' duration would be included in the study.

c. Laboratory studies: Laboratory studies: Na, K, Cl, CO₂, BUN, Hct on admission and at 6, 24, and 48 hours. Stool culture - Shigella, Salmonella and Campylobacter, O&P (every other day, times three), Stool - rotazyme. Record strict input and output. Weight at admission, 24 and 48 hours. This will be accomplished for all patients.

Treatment Group A: (Even social security number) - Standard intravenous therapy: intravenous bolus normal saline (NS) of 10cc per kilogram, then intravenous - D₅ 1/3 Normal Saline + 20 milliequivalent potassium per liter to replace dehydration over 24

hours (potassium to be added only after first void) then continued intravenous fluids at maintenance until: 1) two or less diarrhea stools in 24 hours or less than 10cc stool per kilogram per 24 hours, and 2) normal electrolytes, then

12 to 24 hours Pedialyte, then
24 hours 1/2 strength Isomil, then
Full strength Isomil and puree as appropriate for age
Discharge when stable on full strength Isomil greater than 12 hours.

Greater than 10% dry, give 20cc per kilogram normal saline bolus and, if stable, start replacement fluids as above.

Treatment Group B:

(Odd social security number) - oral rehydration solution: If less than 10% dehydrated and not shocky in appearance start WHO - ORS by mouth to replace estimated dehydration losses over 24 hours.

Then continue ORS at maintenance until 1) two or less diarrhea stools in 24 hours or less than 10cc stool per kilogram per 24 hours, and 2) normal electrolytes, then

24 hours 1/2 strength Isomil, then
24 hours full strength Isomil and puree as appropriate for age.
Discharge when stable on full strength Isomil greater than 12 hours.

If greater than 10% dehydrated or shocky, give 20cc per kilogram normal saline (NS) IV bolus - if patient then appears stable, start ORS as noted above.

Significant stool losses will be replaced on a volume for volume basis in both groups.

Criteria for failure: Patients will be considered to have failed on oral rehydration if they will not take oral fluids, if marked signs of initial dehydration persist beyond eight hours, or if evidence of dehydration returns during maintenance therapy. If a patient fails therapy with oral electrolyte solution, he will be treated with standard IV therapy as in Group A.

6. Data analysis: The following items will be compared using Student's t-test analysis:

- a. Total number of days hospitalized.
- b. Cost of care
- c. Change in weight during hospitalization; measured at 6, 12 and 24 hours after beginning of therapy.
- d. Changes in laboratory values.

e. Complication rate - Complications reported with IV therapy include infection, overhydration, and skin damage secondary to IV infiltration. Complications reported with oral therapy include failure of therapy as defined above, hypo and hypernatremia, and overhydration. Complications may be better compared using a chi square analysis.

Progress:

Principal investigators transferred. Results as of April 1984 indicated oral electrolyte solution was satisfactory in comparison to the standard iv therapy. Inadequate data recording precluded more formal comparison of data, other than that presented by Dr Segapeli in a resident paper. Recommend terminating.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/48 Status: Ongoing

Title:

Use of an Enzyme-Linked Immunosorbent Assay(ELISA) for Detection of Microalbuminuria

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC Richard A. Banks, MC

Dept/Sec: Dept Pediatrics

Assoc Investigators

Key Words:

ELISA; Serum albumin

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To evaluate the reliability of an ELISA in measuring microalbuminuria in patients with insulin-dependent diabetes mellitus (IDDM), in an effort to detect early changes in renal integrity.

Technical Approach:

There will be several phases in the overall investigation which is proposed. The initial phase will be the development of a reliable and sensitive ELISA for urinary albumin in the range of 10-1000 ng/100 ul. ELISA has been shown to detect antigen concentrations down to 1 ng/ml. Specifically, an attempt will be made to develop both a direct competition and double antibody sandwich assay as described in a standard methods manual for ELISA.

A direct competition ELISA will be performed by attaching anti-human albumin to the microplates with a coupling buffer, and then overlaying these with an unknown amount of unlabelled albumin and a known quantity of horse-radish peroxidase (HRP)-tagged albumin. In the double antibody sandwich technique, goat anti-human albumin is attached to the plates, overlayed with an unknown quantity of albumin. This is washed off after a fixed period and rabbit anti-human albumin antibody added. After incubation, this is removed and goat anti-rabbit immunoglobulin antisera tagged with HRP is added. In both assays a substrate is added and the color change, which occurs, is quantitated. Standard curves are then drawn up.

After the procedures have been established, reproducibility and recovery studies using the scheme outlined by Barnett et al will be performed. This consists of 20 once-a-day analyses of a standard aqueous solution of human albumin, and recovery studies in triplicate at three different levels. A protein determination using the BIORAD Kit will be done at the same time to serve as the reference method. Once sensitivity and reliability have been investigated, one of the techniques will be selected for the next phase.

If the initial phase is successful, urine samples obtained from patients with IDDM will be studied. To ensure the availability of adequate samples, aliquots of 24-hour urine collections will be obtained on pediatric patients with IDDM who are followed by the Pediatric Endocrine Clinic WBAMC and University of Florida, Gainesville. These samples will be submitted for analysis of microalbuminuria, creatinine, and beta-2-microglobulin. A separate protocol will be submitted prior to initiation of this phase of the study.

Progress:

Difficulties have been encountered in the initial ELISA determinations. New reagents should eliminate the problem. The study is ongoing.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/08 Status: Ongoing
Title:

Effects of Ritalin on Self-Concept of Children with Attention Deficit Disorder and Hyperactivity.

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Melvin L. Cohen, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Ritalin
Attention Deficit Disorder

MAJ P.C. Kelly, CO
MAJ A.W. Atkinson, MD
DR. Owen Caskey, PhD

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

Objectively measure the effects of Ritalin on the self-concept of children with Attention Deficit Disorder and hyperactivity over a short period of time.

Technical Approach:

In a double-blind approach, patients are treated with Ritalin or placebo for one month and then crossed over. They are tested for self-concept, teacher and parent ratings, and performance on the Gordon Diagnostic System and Central Auditory Processing functions before any medication is given, as well as while on both Ritalin and placebo.

Progress:

A total of 30 patients are necessary for the study. At present, 13 patients have been enrolled. Of these, six have completed all aspects of the study, two more have dropped out for various reasons, and the remaining five patients are in the middle of the study protocol. Several more patients have been selected recently for admission to the study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/16 Status: Completed
 Title:

Comparison of Acoustic Reflectometry with Pneumatic Otoscopy,
 Impedance Tympanometry in the Detection of Middle Ear Fluid.

Start Date: Est Comp Date:
 Principal Investigator: Facility:

COL R.M. Lampe, MC

Dept/Sec: Pediatrics Assoc Investigators
 Key Words:

COL M.R. Weir, MC

Reflectometry

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: Review Results

Study Objective:

Measurement of acoustic reflectometry (AR) will be compared to
 impedance tympanometry, pneumatic otoscopy and results obtained by
 tympanocentesis to determine if acoustic reflectometry is
 sufficiently sensitive to detect middle ear fluid.

Technical Approach:

Pneumatic otoscopy, impedance tympanometry, and acoustic
 reflectometry will be performed on infants and children seen in the
 Pediatric ENT, Ear Followup Clinic, and preoperatively before PE
 tube placement or tympanocentesis. Pneumatic otoscopy will be
 performed using air tight diagnostic otoscope heads with pressure
 generated orally. Impedance tympanometry will be performed using an
 American Tympanometer. Two hundred dependent children will be
 studied, ranging in age from 3 months to 17 years of both sexes.
 They will be patients normally attending the above clinics or
 preoperatively.

Progress:

Acoustic reflectometry, a new technique for detecting middle ear
 effusion (MEE), was compared with results from tympanocentesis or
 myringotomy in 75 patients (141 ears). There was a highly
 significant association for ears having MEE with high reflectivity
 (5 through 9 units) and for ears having no MEE with low reflectivity
 (0 through 4 units). In a pediatric population with MEE present in
 98 of 141 ears and using reflectivity readings greater than 4 to
 indicate MEE, the sensitivity of this technique was 86.7% and the

specificity was 69.8%. False positive errors usually occurred in ears with thick tympanic membranes, or in ears where reflectivity was determined prior to the induction of anesthesia. False negative errors usually occurred in ears with both air and fluid. This technique was validated by direct comparison with tympanocentesis or myringotomy and can be used with pneumatic otoscopy and impedance tympanometry to follow children with MEE. This project has been completed and presented in part as an exhibit at the AAP Fall Meeting. Accepted for publication in Pediatrics.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/25 Status: Ongoing
Title:

Adolescent and Pediatric Care Delivery at Army Medical Treatment Facilities

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ W.K. Imai, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Care Delivery

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

This study will characterize health care delivery to dependent children in Army Medical Treatment Facilities. It will delineate the extent to which we make care available to adolescents, and in so doing, serve as a guide to pediatric training programs and treatment facilities.

Technical Approach:

We proposed to study the current status in order to better prepare the training programs and the trainees for the future, as well as an aid to individual MTF's for optimum provision of adolescent and pediatric health care.

Subjects: Fifty-seven Pediatric and Family Practice Services at MEDDAC's and six medical center Adolescent Medicine Services.

Phases: Survey distribution and collection. Collation and interpretation of results. Service specific survey forms will be utilized. No controls are necessary.

Progress:

Data has been collected and analysis is in progress.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/61 Status: Completed
Title:

An Explanatory Study of the Exceptional Family Member Program

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ A.W. Atkinson, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words: MAJ R.H. Gemmill, MSC

Exceptional family member

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

The purpose of this explanatory study is twofold: First to describe characteristics of the exceptional family member population. Second, to study how Army active duty personnel with exceptional family members perceive the exceptional family member program.

Technical Approach:

A questionnaire will be distributed to all adult soldiers who voluntarily come to the Pediatric Clinic to initiate processing for the Exceptional Family Member Program

Progress:

Over 50 questionnaires have been returned to the associate investigator and he is beginning to work up the study. We should have results in early 1985.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/64 Status: Ongoing
 Title:

Use of the Gordon Diagnostic System to Measure Changes in Attention Deficit Disorder Treated with Ritalin.

Start Date: Est Comp Date:
 Principal Investigator: Facility:

MAJ Melvin L. Cohen, MC

Dept/Sec: Pediatrics Assoc Investigators
 Key Words:

Attention Deficit Disorder

MAJ P.C. Kelly, DO
 MAJ A.W. Atkinson, MC

Accumulative MEDCASE Est Periodic
 Cost OMA Cost: Review Results

Study Objective:

It is often difficult to determine, clinically, the appropriate dose of Ritalin for children with Attention Deficit Disorder. This study will assess the ability of the Gordon Diagnostic System to measure improvement or deterioration in children with ADD who are treated with Ritalin.

Technical Approach:

Thirty children with ADD and hyperactivity will be given either placebo or Ritalin in double blind fashion. In addition to studies already planned, each child will be tested with the GDS at the time his diagnosis is initially confirmed. He will be tested again after one month of Ritalin or placebo, and a third time one month after the crossover occurs. Using a special commercial computer program, both tasks of the GDS will be analyzed for variation of performance during the test period. Results will be compared for the following parameters: Delay task - (a) rewards, (b) responses, (c) efficiency ratio; and for the vigilance task - (a) correct responses, (b) omissions, (c) commissions, and (d) task monitoring data. These data will be compared for response on or off medication.

Progress:

Twelve patients have been enrolled in the study. Two additional patients were enrolled, but have been suspended due to noncompliance. Of the enrolled patients, four have totally finished the study, but results have yet to be tabulated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/65 Status: Ongoing
Title:

Diagnosis of Attention Deficit Disorder Using a New Objective Measure of Impulsivity and Sustained Attention

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ A.W. Atkinson, MC

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Attention Deficit Disorder

MAJ P. Kelly, MC
MAJ M. Cohen, MC
MAJ B. Ting, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To assess the ability of the Gordon Diagnostic System (GDS) to diagnose attention deficit disorder (ADD) compared to standard, customary procedures used in developmental pediatrics.

Technical Approach:

Military dependent children between six and eleven years of age referred to the Developmental Pediatric Clinic by parents, physician, or school for evaluation of school or behavior problems will be voluntarily enrolled in the study. In addition to customary evaluation procedures, the child will be evaluated with the GDS (approximately 17 minutes). Developmental and medical history, neurodevelopmental examinations, observations, teacher, and parent behavioral questionnaires, and consultations, as needed, will be used to make the diagnosis (according to the DSM III) and formulate a management plan as usual. Use of stimulant medication will be based solely on customary diagnostic criteria. Testing with the GDS will be repeated twice at two month intervals, and once more six months from the start. Using a special commercial computer program, both tasks of the GDS will be analyzed for variation of performance during the test periods (four, two minute blocks for delay and three, three-minute blocks for vigilance tasks). Results will be printed in numerical lists as well as bar graphs for the following parameters. Delay task - (a) rewards, (b) responses, (c) efficiency ratio; and for the vigilance task - (a) correct response, (b)

omissions, (c) commissions, and (d) task monitoring data. These data are used in identifying differential responses of individual patients. Response to management will be judged in the routine fashion using standardized questionnaires as well as history and performance in school. The project will run until a minimum of fifty children with the diagnosis of ADD/ADD-H have been evaluated and followed for six months. At that time data will be collated from all patients to assess the following: (1) comparison of clinical diagnoses of ADD/ADD-H with performance on GDS, (2) comparison of all children 'diagnosed' by GDS as ADD with their clinical assessment, (3) for all children treated with stimulant medication, a comparison of their GDS scores before and after treatment, looking for correlations with positive and adverse responses, and (4) correlation of teacher/parent questionnaires with results on the GDS. Data will be analyzed statistically by a multivariate analysis of variants.

Progress:

Thirty-six patients have each been evaluated at least once. Preliminary review of this data is pending. We expect that a total of 50 patients will be enrolled with a diagnosis of ADD.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/69 Status: Terminated
Title:

The Use of the Gordon Diagnostic System (GDS) for the Early
Diagnosis of Attention Deficit Disorder (ADD)

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ P.C. Kelly, DO

Dept/Sec: Pediatrics Assoc Investigators
Key Words:

Gordon Diagnostic System MAJ A.W. Atkinson, MC
MAJ B. Ting, MC
MAJ M.L. Cohen, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

ADD is estimated to occur in 5-10% of school aged children without intervention. Children with this disorder fail chronically at academic tasks. This condition has been associated with low self-esteem, poor self-image, depression, and academic lag. This study is being done to determine if the GDS is useful as a screening tool for the early detection of children with ADD.

Technical Approach:

All military dependent children entering first grade at Milam School in September 1984 (approximately 60-80) would be tested using the GDS. Milam school is an elementary school in the El Paso School District.

In early December 1984 the teachers will be asked to complete the ACTers Scale on all children in the study. In early December the parents of all subjects will be asked to complete the Hyperkinesis Index and a brief questionnaire developed by the investigators. The parents of all children who have evidence of ADD on the basis of the ACTers Scale, the Hyperkinesis Index, or the GDS will be contacted and an appointment made for a developmental pediatric evaluation. All parents who respond positively to questions on the questionnaire will be contacted for an appointment in the clinic. Data will be analyzed statistically using a multivariate analysis of variants.

Progress:

The El Paso Independent School District turned the protocol down; they felt this involved too much teacher-time and would not benefit the El Paso School District. An appeal was sent by Owen Caskey, Psychologist NE District, civilian investigator, with no response to the appeal. The study has been cancelled; it will be reinstituted if the schools reconsider.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/02 Status: Completed

Title:

Analysis of a Model to Assess the Impact of Automation on Pharmacy Related Services.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT Bryan L. Mercer, MSC

Dept/Sec: Pharmacy

Assoc Investigators

Key Words:

Automation

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

Identify intellectual abilities required for performance of specified tasks involved in drug related services. Determine the likelihood of automating the intellectual abilities described in Guilford's Structure of Intellect. Identify automation likelihood characteristics of pharmacy tasks by synthesis of results. Classify tasks into high-low automation likelihood groups. Assess potential impact on pharmacy related services resulting from automation. Discuss the automation likelihood of those tasks which pharmacists felt were important to their practice as reported in the National Study of the Practice of Pharmacy.

Technical Approach:

Subjects in this study will complete one of two questionnaires. The first group will be composed of pharmacy professors in colleges of pharmacy in the United States as identified in the faculty listing of the American Association of Colleges of Pharmacy. Only professors listed in Pharmacy Administration and Management and Pharmacy Practice will be asked to participate initially. The second group will be composed of solicited computer science professors and researchers. Members of the Special Interest Group on Biomedical Computing and the Computer Science and Engineering Research Study Steering Committee will be asked to participate initially. Data will be analyzed to determine which intellectual abilities are required to perform what pharmacy tasks. Intellectual abilities will be ranked from most frequently chosen to least frequent. Utilizing the automation estimates in association with these frequency distribution will aid in determining which tasks lend themselves to automation.

PROGRESS:

Questionnaires have been received and data analyzed. A manuscript is in preparation detailing results.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 81/37 Status: Terminated

Title:

Torque and Its Relationship to Academic Achievement and Behavior in Children

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ T.B. Jeffrey, MSC

Dept/Sec: Psychology Svc

Assoc Investigators

Key Words:

Torque

LTC P. LoPiccolo, MC
Mr Thomas D. Carter, Jr, M.Ed

Accumulative MEDCASL

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To evaluate the relationship between torque, academic achievement and behavior in children.

Technical Approach:

One hundred children between the ages of 9 and 13 seen in the Pediatric Outpatient Clinic will be evaluated with the following instruments: Torque Test, Wide Range Achievement Test (Jastok, Bijour, and Jastok, 1963), Connor's Abbreviated Teacher Rating Scale, the Burk's Behavior Rating Scale, the Peabody Picture Vocabulary Test, and selected portions of Reitan's Lateral Dominance Examination.

The Peabody Picture Vocabulary Test correlates at a high level (Range = .63 - .87) with intelligence scales and requires only a few minutes to administer and score. Groups will be matched (torque versus nontorque) for level of intellectual functioning.

The results of the Torque Test will be scored by employing a single blind procedure. Data will be analyzed dichotomously (torque versus nontorque) to determine if a relationship exists between torque, lateral dominance, academic achievement, and behavior through a multivariate analysis of variance paradigm (2x3x2x2 factorial design). It is hypothesized that those with torque will display mixed lateral dominance on Reitan's test. It is also hypothesized that those with torque will do less well as measured by academic

achievement than their torque-free peers. A third hypothesis is that those with torque will have more behavioral problems as perceived by teachers and parents than their torque-free peers.

Progress:

A total of 41 patients were entered into the study with no untoward occurrences. The principal investigator requested the study be terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/29 Status: Completed

Title:

Hypnosis for the Treatment of Smoking Cessation

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC T.B. Jeffrey, MSC

Dept Psychiatry/Psychology Svc

Dept/Sec: Dept Psychiatry/Psychology Sv Assoc Investigators

Key Words:

Smoking cessation; hypnosis

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To evaluate the efficacy of several variables in the treatment of smoking cessation.

Technical Approach:

A number of therapeutic approaches are utilized in the active smoking cessation program in the Psychology Service. Common to all is an underlying reliance on clinical hypnosis. A systematically varying difference among various practitioners providing smoking cessation treatment will be used. These variables are dual versus single induction, group versus individual treatment, exclusion versus nonexclusion therapy, and high versus low anxiety. Support is available in the literature to justify each of the aforementioned variables for the treatment of this problem. Controlled outcome studies on the efficacy of these variables is anticipated.

Progress:

Fifty-eight patients were entered with no problems encountered. A manuscript is in preparation for submission to a medical journal.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/67 Status: Ongoing
Title:

Psychological and Physiological Effects of Didactic Instruction and Relaxation Training with Essential Hypertension Patients

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T.B. Jeffrey, MSC

Dept/Sec: Psychology Svc Assoc Investigators
Key Words: MAJ G.R. Greenfield, MSC
Relaxation Training MAJ C.L. Ferguson, MC
Randy G. LaGrone, M.A.

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To compare the relative effects of didactic instruction and relaxation training on the systolic and diastolic blood pressures of essential hypertension outpatients.

Technical Approach:

Subjects will be randomly assigned to one of three groups: didactic instruction only, didactic instruction with relaxation training, and no treatment control. The two treatment groups will receive eight sessions of didactic instruction four times weekly for 30 minutes. Lectures will be presented on stress management, diet, exercise, and substance abuse. This instruction is intended to modify dysfunctional behaviors known to be associated with essential hypertension. The didactic instruction only group will participate in an additional 45 minutes each day of discussion on each lecture topic and supportive counselling. The didactic instruction with relaxation training group will receive an additional 45 minutes each day of discussion on each lecture topic, supportive counselling and relaxation training. In addition, this group will be provided with a modified progressive relaxation audio tape for home practice. The control group will receive no treatment or instruction. The dependent variable measure, BP, will be recorded independently of the treatment conditions (pre-, post, and followup) by staff in the hypertension clinic at routine appointments. Psychological measures will be administered at pre (MMPI, Medication side effect index, quality of life scale, Harvard group scale of hypnotic

susceptibility) and post-treatment (Jenkins activity survey). Demographic and psychological data will be studied for their relationship to differential treatment effects. A health habits questionnaire will be used at followup to assess the impact of didactive instruction on targeted behaviors.

Progress:

Reductions in staffing of the Psychology Service and increasing patient demand has delayed the initiation of this study. We are currently planning to begin in late November 84.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/79 Status: Ongoing
Title:

Burn-Out Prevalence in Health Care Personnel

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T.B. Jeffrey, MSC

Dept/Sec: Psychology Svc Assoc Investigators
Key Words:
Burn-out MAJ G.R. Greenfield, MSC
MAJ W.F. Barko, MSC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To determine the prevalence of job-related burnout in health care personnel at William Beaumont Army Medical Center.

Technical Approach:

This prevalence study will use the MBI to measure three dimensions of burnout (emotional exhaustion, personal accomplishment, and depersonalization) among selected staff at WBAMC.

a. Random sampling of 50% of civilian, officer, and enlisted staff will be obtained from the authorized and assigned roster of all personnel and distributed through normal hospital channels. Questionnaires will be numbered for control purposes to assist in securing a 75% return rate, but all information will be reported anonymously.

b. Questionnaires will be analyzed through descriptive statistics. Parametric statistics will be employed to evaluate measures of central tendency and distribution of scores for:

- (1) Prevalence of burnout.
- (2) Comparative levels of burnout within sample populations.

Progress:

A random sample of 50% of WBAMC civilian, officer, and enlisted staff completed the MBI (Burn-Out Measure) and a demographic questionnaire. There was an approximate 72% return rate. The data is currently being typed into the computer for analysis.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 82/42 Status: Terminated

Title:

Clinical and Surgical Correlation Between Computerized Axial Tomography (CT) vs Metrizamide Myelography in the Patient with Low Back Pain.

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

CPT W.V. McAbee, MC

Dept/Sec: Dept Radiology

Assoc Investigators

Key Words:

CAT; Metrizamide Myelography

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To compare which method (CT or metrizamide myelography) has the greatest degree of correlation with surgical and clinical findings in the low back patient and to determine the strengths and weaknesses of both modalities.

Technical Approach:

The study will consist of 100 low back pain patients that would ordinarily receive a metrizamide lumbar myelogram at our institution and who subsequently go to surgery. Initially the patient will receive a lumbar CT scan.

1. Areas to be scanned will coincide with regions of clinical suspicion.

2. IV contrast will be given in bolus form of 100cc (Conray 60).

3. CT cuts at 5 mm thickness spaced at 5 mm distances from the bottom of the superior pedicles to the top of the inferior pedicles of the involved disc space.

4. The doctor performing the study will read the film routinely with available clinical information

5. The film will be read "blindly" by one of the clinical investigators without clinical information filling out the protocol CT form.

Metrizamide myelogram will follow the CT scan.

1. 15cc of 190 mg/cc of metrizamide will be injected into the subarachnoid space.
2. AP, lateral, oblique and cross table lateral decubitus films will be obtained.
3. The doctor performing the study will read out the film with all the clinical information available.
4. The film will be read by one of the clinical investigators without clinical information and he will fill out the protocol myelogram form.

Clinicians will be asked to fill out a clinical information sheet before the performance of any exam. The sheet should include: 1) probable levels of involvement, 2) degree of clinical suspicion, 3) brief history and pertinent physical findings, 4) the surgeon will be asked to comment on the nature of the surgical findings to include:

1. Nerve root impingement and type.

- Hypertrophied facet
- Hypertrophied ligamentum flavum
- Bulging disc
- Free fragment
- Other

2. Amount of saline injected into involved disc.

3. Did he find what he expected on the basis of the CT and myelogram at surgery.

Progress:

No progress reported on this study. Principal investigator has resigned, and the study terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 78/03 Status: Ongoing

Title:

National Intraocular Lens Implantation Study

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

MAJ Antonio San Martin, MC

Dept/Sec: Surgery, Ophthalmology

Assoc Investigators

Key Words:

Intraocular lens

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To participate in the study of clinical results of implantations of intraocular lens organized by the Intraocular Lens Manufacturer's Association in response to directives of the Ophthalmic Classification Panel, FDA.

Technical Approach:

An intraocular lens is a prosthetic replacement for the eye's crystalline lens. It is placed in the eye at the time of cataract surgery, where it is fixated by a variety of means, with the intention that it remain permanently and correct the large refractive error remaining after conventional cataract surgery.

PROGRESS

One hundred sixty-seven intraocular lenses were implanted in FY84 with no adverse effects due to implantation. The project is ongoing.

Detail Summary Sheet

Date: 1 Oct 84 Protocol No: 81/07 Status: Terminated
Title:

Comparison of Mortality and Morbidity of Uretero-
ileocecosigmoidostomy With Other Urinary Diversions

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL F.L. Diaz-Ball, MC

Dept/Sec: Surgery/Urology Assoc Investigators

Key Words:
Ureteroileocecosigmoidostomy

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

At present the urinary diversion methods accepted as effective have been the ones which require an external appliance over a stoma and on occasion ureterosigmoidostomy. Examples among these are: The ileal loop or conduit of Bricker, ileocecal loop, or the colonic loop. All these are prone to complications and are less ideal. In 1972 the senior investigator and associates reported on a study in dogs alone at Letterman Army Medical Center in which the feasibility of an internal diversion using a uretero-ileocecosigmoidostomy was established. The anti-reflux action of the ileo-cecal valve can be enhanced with the newly developed Zinman technique. Prior to a wide application in humans, we should prove that the incidence of complications is comparable or preferably less than the accepted methods used at this time. It is projected to perform surgery in control groups of ileal loops, colonic loops, ureterosigmoidostomies and compare incidence of complication with equal numbers of uretero-ileo-cecosigmoidostomies.

Technical Approach:

1. Control Group I - a series of 6-12 dogs will undergo ileal loop diversion.
2. Control Group II - a series of 6-12 dogs will undergo a colonic loop.
3. Control Group III - a series of 6-12 dogs will undergo a ureterosigmoidostomy.

4. Tested Group IV - a series of 6-12 dogs will undergo uretero-ileocecocolostomies.

Data Collection:

Preoperative: Will include serum creatinine, BUN, and CBC. Urine C and S if possible, IVP and R.C. Barium enemas would be performed to establish functional integrity of urinary and bowel tracts including ileocecal valve competence. Kidney biopsy for regular and electron microscopy. **Intra-operative:** serum creatinine,, BUN, urine from renal pelvis or ureters for C and S, urine aspirates from bladder for C and S.

Postoperative: Every 1-2 weeks BUN and creatinine. Every month an IVP, and every 2 months a cystogram. Will be as in humans with IVs until safe to feed, etc. At least every 1-2 weeks repeat CBC, BUN, creatinine, retrograde cystogram every month times 3 and then every three months times 3.

Long Term: Dogs will be kept ideally at least one year alive, facilities permitting. At that time they could be sacrificed, autopsied for detection of changes due to surgery in the urinary system and other systems.

Control Groups I and III, and the test group will comprise the initial study. If time and funding permit, Control Group II, and possibly another group with ileo-cecal cutaneous diversion, may be compared to the tested group.

PROGRESS:

Approximately 17 dogs have undergone two separate procedures, the results of which are in the process of being compared. Data is being compiled for manuscript preparation.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/03 Status: Terminated

Title:

The Use of Digital Subtraction Venous Angiographs in Differential Diagnosis of the Traumatically Widened Mediastinum

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC R.J. Lewis, MC

Dept/Sec: Dept Surgery

Assoc Investigators

Key Words:

Digital Subtraction, Venous Angiographs

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To assess the accuracy of digital subtraction venous angiography in the diagnoses of injury to vascular structure in the traumatized, widened mediastinum.

Technical Approach:

All patients who arrive in the Trauma Unit with a history of severe trauma and who are found to have a widened mediastinum by chest x-ray (PA or an upright 6 ft AP film) will undergo, in addition to the usual arteriography, digital subtraction venous angiography in order to assess its accuracy in such instances by comparing it with the known accuracy of the former method. To prevent bias on interpretation, each method will be interpreted by separate "blinded" radiologists.

Progress: No patients were entered into this study before the principal investigator was assigned a long-term TDY OCONUS and subsequently reassigned.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/05 Status: Terminated

Title:

The Efficacy of Routine Monitoring for Early Occult, Post-Traumatic Deep Venous Thrombosis by Noninvasive Phleborheography

Start Date:

Est Comp Date:

Principal Investigator:

Facility:

LTC R.J. Lewis, MC,

Dept/Sec: Dept Surgery

Assoc Investigators

Key Words:

Thrombosis; phleborheography

Accumulative MEDCASE

Est

Periodic

Cost

OMA Cost:

Review Results

Study Objective:

To assess the efficacy of routine monitoring for early occult post-traumatic deep venous thrombosis.

Technical Approach:

All patients admitted to the Trauma Unit with any and all injuries would be included in the study. The Grass Phleborheography represents a noninvasive method of measuring and recording deep venous flow in the lower extremities. Each patient would be tested twice daily (morning and evening) with recordings of both extremities to determine venous patency. Periodic arterial blood gases would also be followed. Any patient "positive" for suspected deep venous occlusion would be examined by venography to confirm the diagnosis.

Progress:

No patients were entered into this study before the principal investigator as assigned a long-term TDY OCONUS followed by a permanent reassigned.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/16 Status: Ongoing

Title:

Size of the Abdominal Aorta: In vivo vs Ultrasonic Measurement

Start Date:

Est Comp Date:

Principal Investigator:
LTC Silverio Cabellon,MC

Facility:

Dept/Sec: Dept Surgery

Assoc Investigators

Key Words:

Abdominal aorta

Accumulative MEDCASE
Cost

Est
OMA Cost:

Periodic
Review Results

Study Objective:

To determine the size of the normal abdominal aorta. To determine the accuracy of ultrasound in measuring the size of the normal abdominal aorta.

Technical Approach:

Measure by caliper the infrarenal aorta at surgery for other abdominal conditions; compare with size determined by ultrasound before or after surgery.

Progress:

Project will be restarted in November 84. Projected completion date is December 1985.

Detail Summary Sheet

Date: 1 Oct 84	Prot No: 83/22	Status: Completed
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Title:

Comparison of Cardiovascular Stability with Fentanyl and Fentanyl-Nitrous Oxide Induction in Patients Undergoing Peripheral Vascular Surgery

Start Date:	Est Comp Date:
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Principal Investigator:
CPT D.D. Gautreaux

Facility:

Dept/Sec: Dept Surgery	Assoc Investigators
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Key Words:

Anesthesia, Fentanyl, Periopheral vascular

CPT C. Callender, CPT
CPT J. Martin
CPT D. Hendryx, 1Lt
1Lt K. Baethge

Accumulative MEDCASE	Est	Periodic
Cost	OMA Cost:	Review Results

Study Objective:

To compare the hemodynamic effects of induction of general anesthesia with fentanyl 12 ug/kg with the hemodynamic effects of induction of general anesthesia with a combination of fentanyl 8 ug/kg and a 50% mixture of nitrous oxide and oxygen in patients having carotid endarterectomy of aorto femoral bypass surgical procedures.

Technical Approach:

The sample population will be approximately ten adult patients, both military and civilian, who are electively scheduled for carotid endarterectomy or aortofemoral bypass graft procedures and who are assessed as not having an airway difficult to manage. Each participating subject will sign a voluntary consent form prior to participating in the study. Subjects will be randomly assigned to one of two treatment groups: Group I will receive fentanyl 8 ug/kg and a 50% concentration of N₂O and O₂ for induction; Group II will receive fentanyl 12 ug/kg for induction. All patients will be premedicated with morphine 0.1 mg/kg and scopolamine 0.005 mg/kg intramuscularly and preoxygenated with 100% O₂ via a Bain (R) anesthesia circuit. Topical application of a 4% solution of lidocaine by laryngoscopy will be given prior to intubation. Each patient will be monitored by electrocardiogram, direct radial artery catheter, and central venous catheter with display via electrical display and waveform monitoring equipment. Data from each of these parameters will be recorded at intervals throughout the induction phase and concluded at the time of surgical incision. Baseline data for each parameter will be recorded prior to the administration of

induction agents. Arterial blood gases will be obtained prior to induction and at fifteen minute intervals through induction to assure steady-state PaCO₂ levels. The paired t-test will be used to statistically analyze the data obtained. NOTE: Monitoring techniques and treatment modalities used for this project are accepted as current standard anesthesia practice. No experimental techniques or modalities will be used in the study.

Progress:

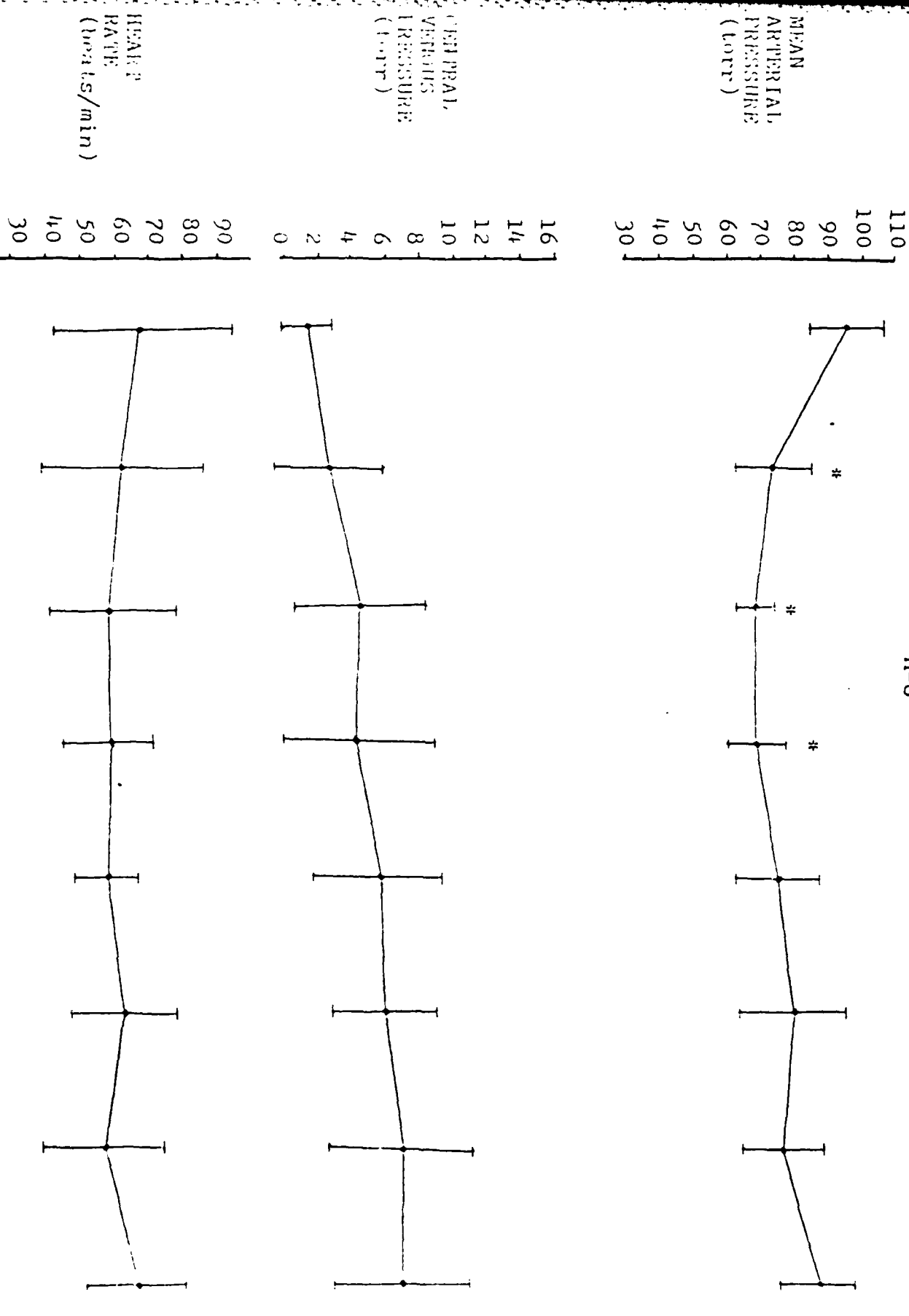
Results are illustrated in the tables. Significant decreases in mean arterial pressure (MAP) were observed in both test groups following narcotic loading. In Group I this drop in MAP occurred immediately following narcotic loading and was maintained until the time of laryngoscopy for laryngo-tracheal anesthetic (LTA) administration. MAP then rose and stabilized in this group with values at skin incision similar to baseline values. MAP also dropped following narcotic loading in Group II, but this drop occurred later in the sequence and was reflected for one collection period only, and then stabilized and returned to baseline levels at time of skin incision. In direct comparison between groups, there was no statistical difference between MAP values during the induction period.

Central venous pressure measurements reflected a gradual rise in both groups during the induction sequence. The rise in central venous pressure was significant in Group II following narcotic loading and was sustained until time of skin incision, when the values returned to baseline levels. Though there was a gradual rise in central venous pressure in Group I during the course of anesthesia induction, there was no value statistically higher than baseline recordings. As with MAP, there was no significant difference in central venous pressure values recorded between groups during the induction sequence.

Heart rate was the most stable parameter observed in both groups. There was no significant change in heart rate during induction in either group, and no significant difference in values between groups over the observation time.

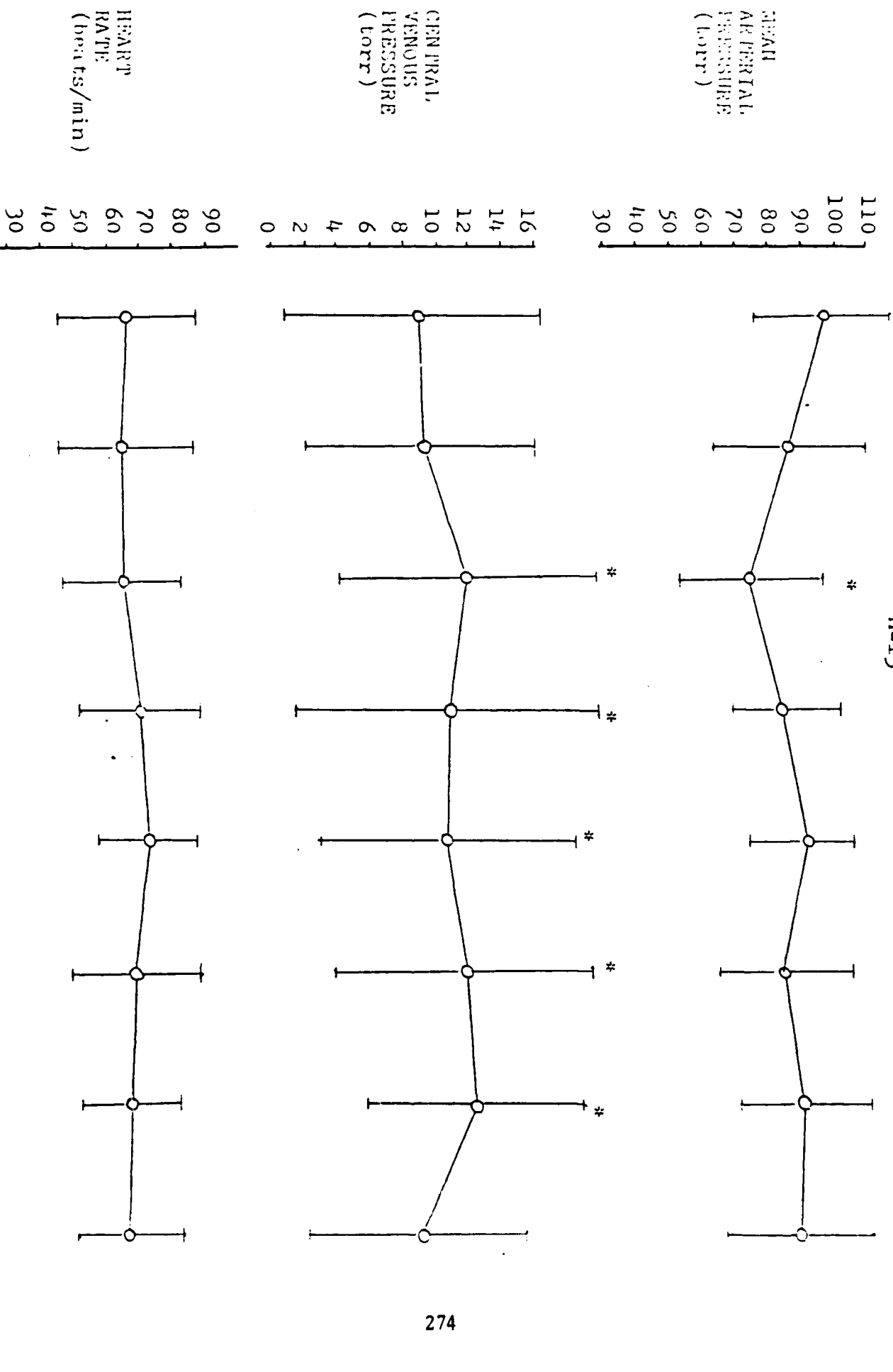
STATUS: Completed. A manuscript has been submitted for publication. CPT Gautreaux received an award for Scientific Achievement at WBAMC for this study.

Group 1 (Penlanyl and N₂O/O₂)
Cardiovascular Responses During Anesthesia Induction
n=6



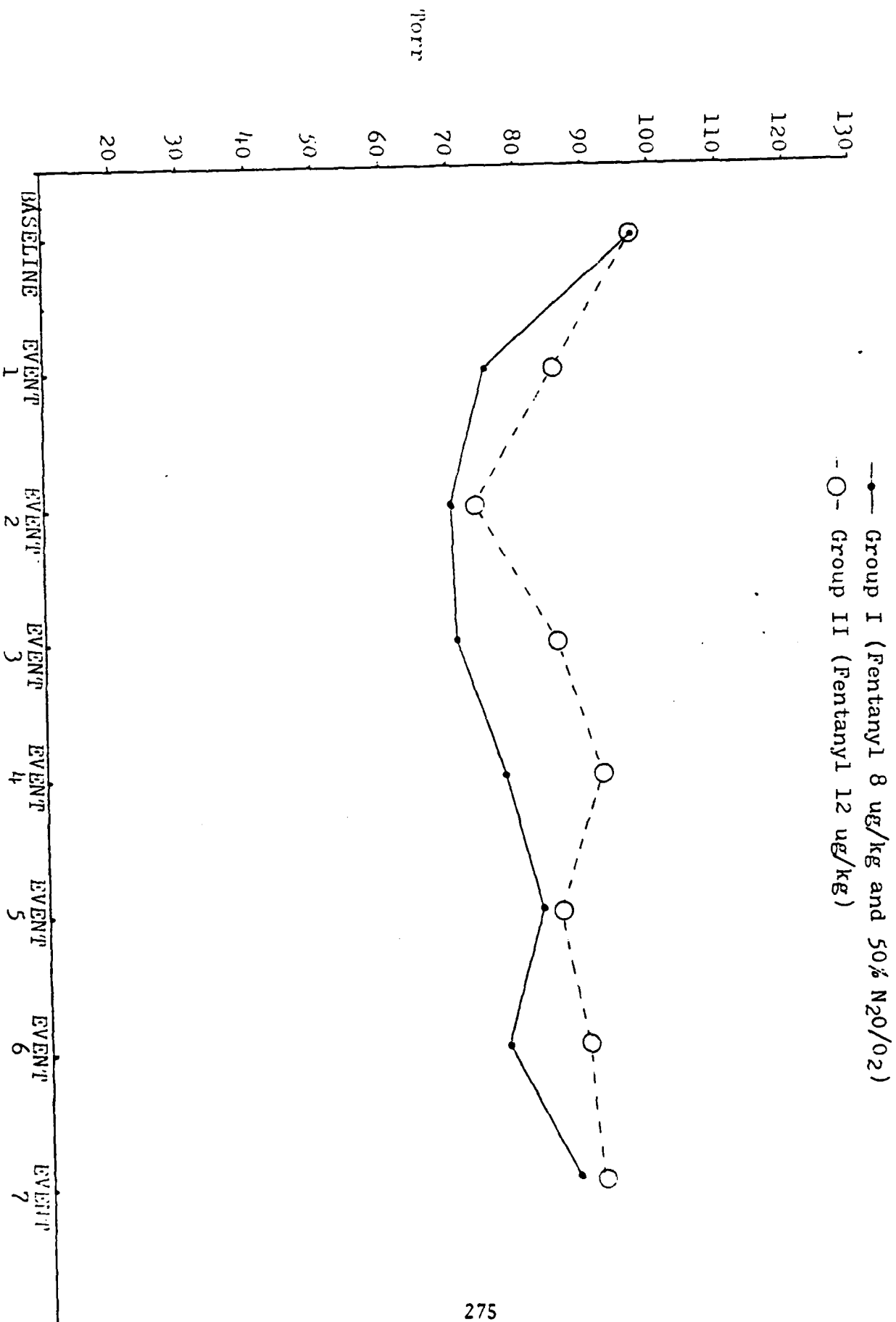
* Indicates statistically significant variation from baseline (alpha=0.05)

Group 11 (Per Anesth)
Cardiovascular Responses During Anesthesia Induction
n=13

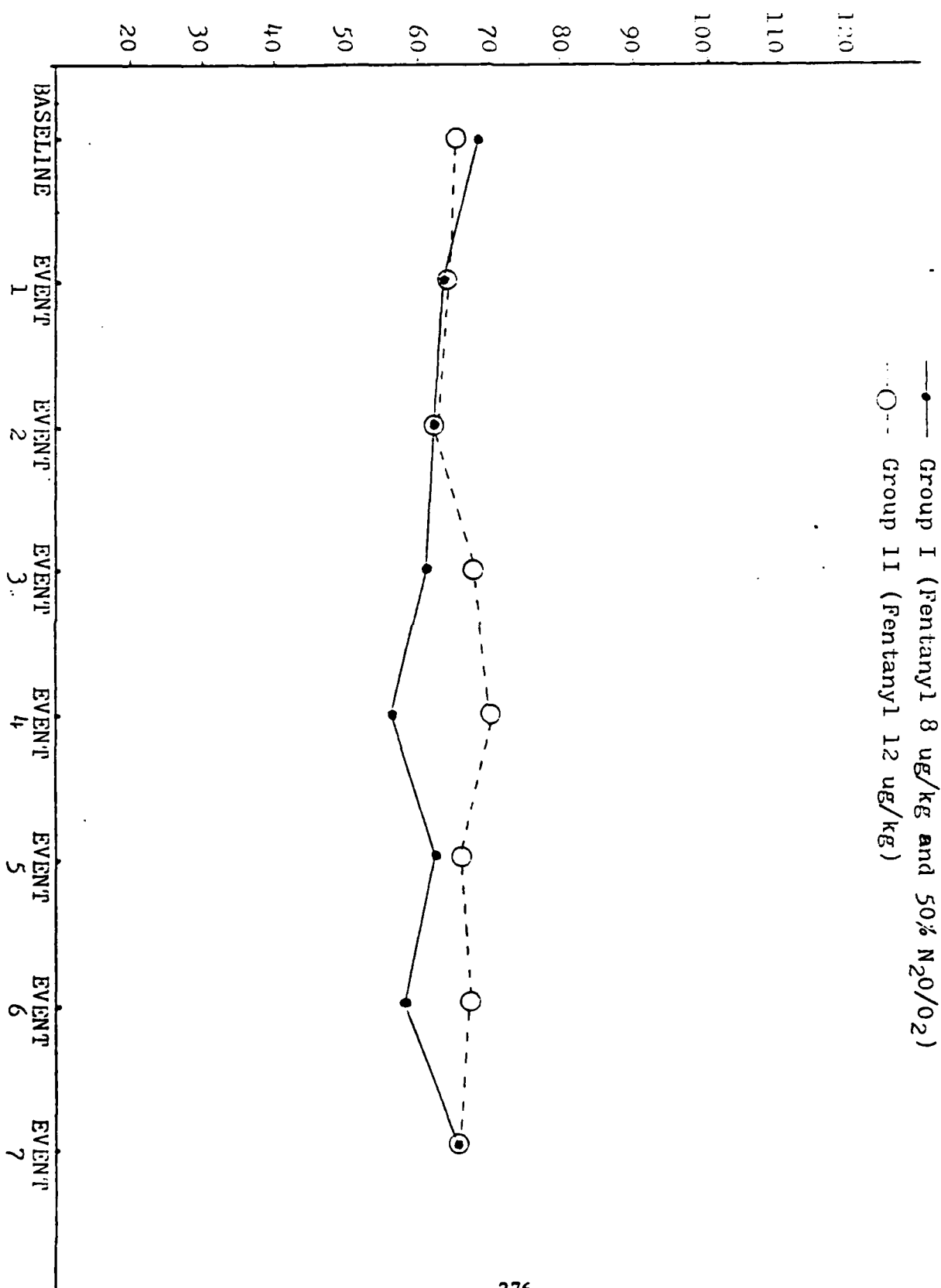


* Indicates Statistically Significant Variation from Baseline (alpha=0.05)

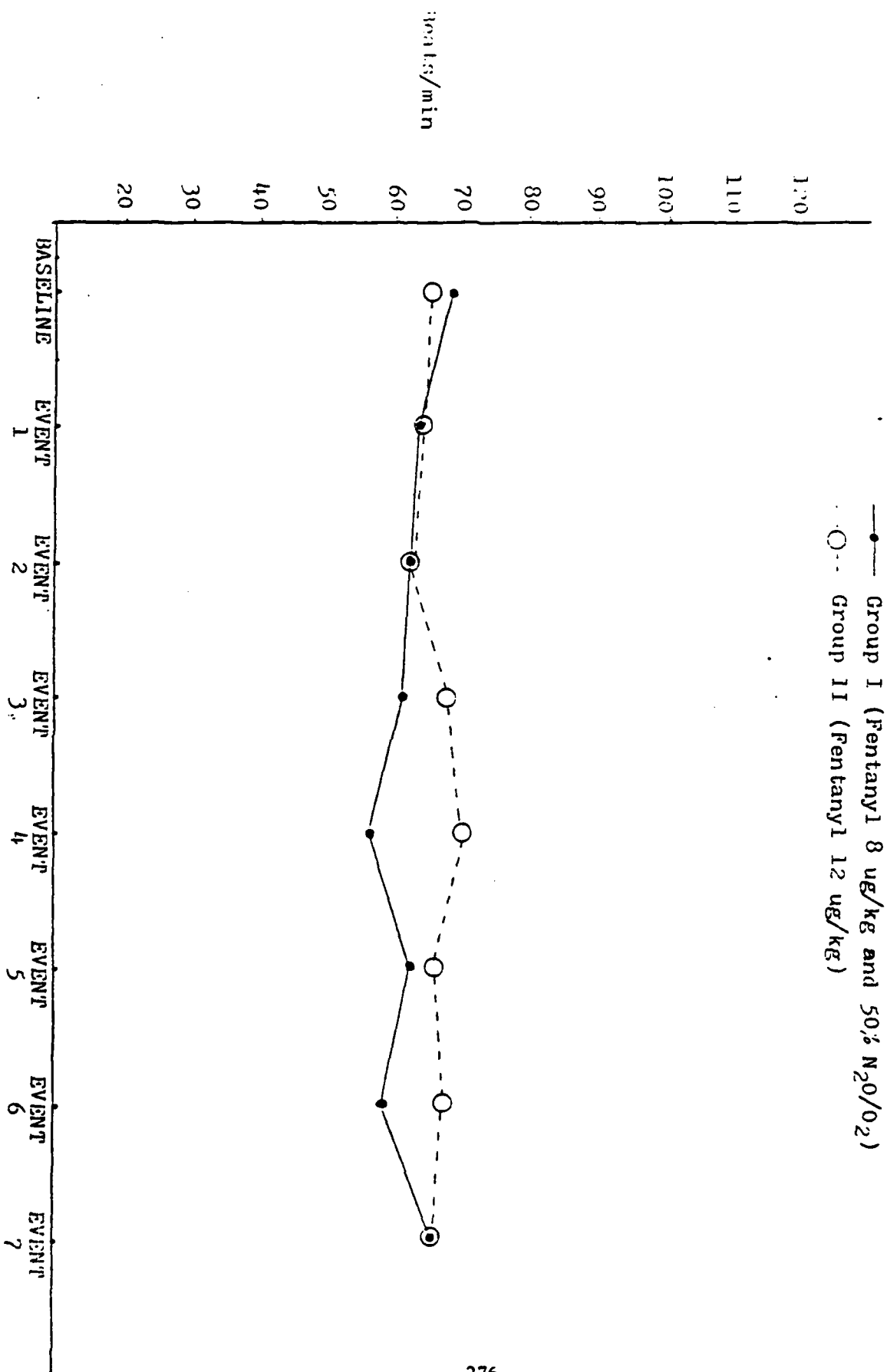
Mean Arterial Pressure During Anesthesia Induction ($\alpha=0.05$)



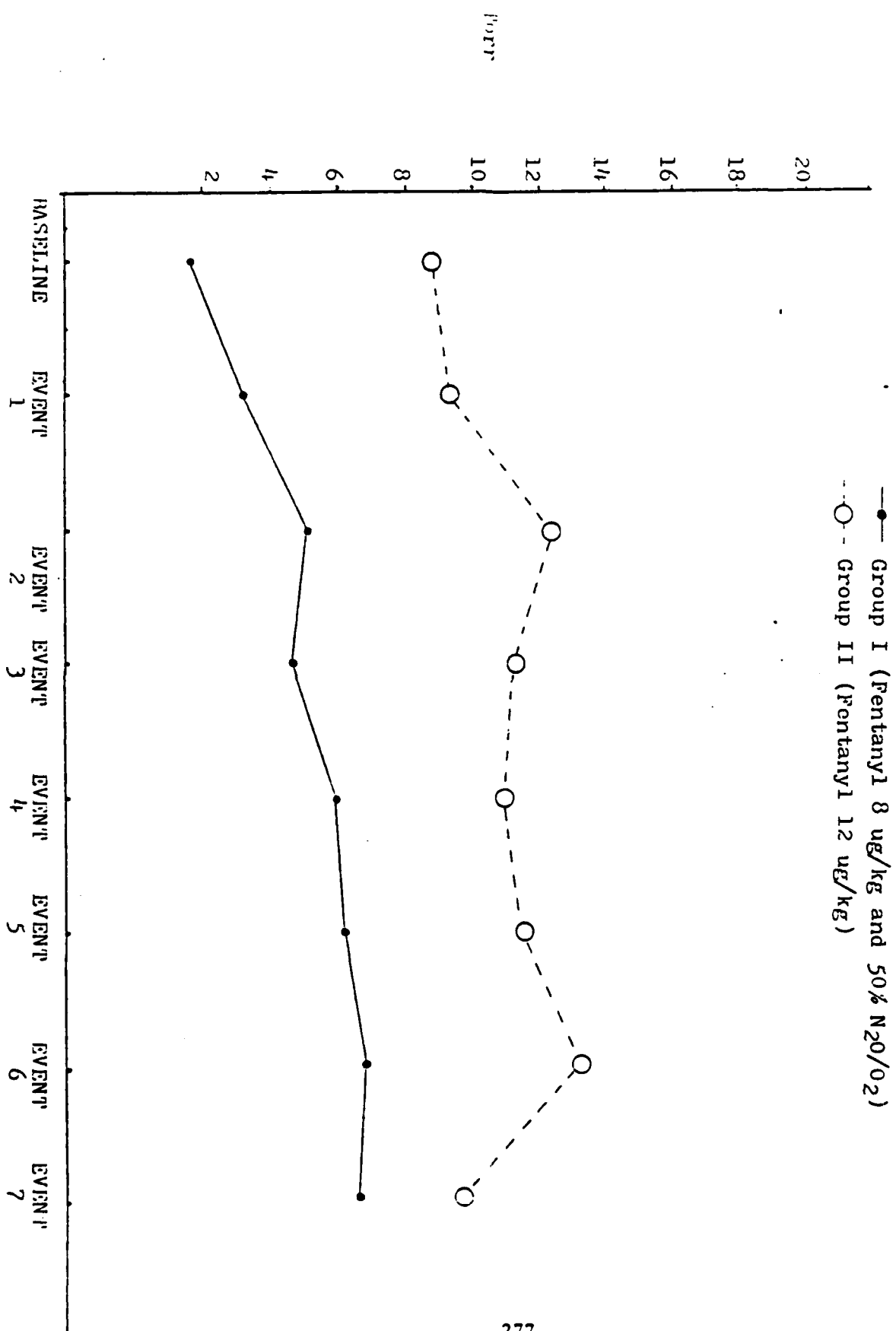
Heart Rate During Anesthesia Induction ($\alpha=0.05$)



Heart Rate During Anesthesia Induction ($\alpha=0.05$)



Central Venous Pressure during Anesthesia Induction ($\alpha=0.05$)



Detail Summary Sheet

Date: 1 Oct 84	Protocol 83/41	Status: Terminated
Title: Autonomous Life of Cancer Cells after Host Separation		
Start Date:	Est Comp Date:	
Principal Investigator: Dr. Sjord Steunebrink, MD,	Facility:	
Dept/Sec: Dept Surgery	Assoc Investigators	
Key Words: Cancer cells		
Accumulative MEDCASE Cost	Est OMA Cost:	Periodic Review Results
Study Objective:		

To prove that cancer cells appear viable after 1, 2, or 3 weeks, in contrast to deteriorated other nonmalignant tissue from host.

Technical Approach:

To take a surgical section without preservative, by pathologist, after one and two weeks of any malignant tissue. Tissue should be free from chemotherapy. Tissue should be exposed to normal outside open air. Any successful finding may lead to exposure of cancer tissue to humid air, anerobic air atmosphere and other testing. Further investigative tests, if appropriate, for which another protocol will be written.

Progress:

Repeat studies were not completed on this study. The principal investigator has departed WBAMC and no one else in the department is interestd in pursuing this study.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 83/47 Status: Terminated
Title:
Levamisole and Vitamin A Therapy in the Prevention of Sepsis in
Multi-Traumatic Patients

Start Date: Est Comp Date:
Principal Investigator: Facility:
COL Ronald A. Lewis, MC

Dept/Sec: Assoc Investigators
Key Words:
Levamisole; Vitamin A

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine the role of levamisole and vitamin A in the prevention of sepsis in multitraumatic patients and to determine the immunopotentiating effects of levamisole and vitamin A as measured by microbial and immunological parameters.

Technical Approach:

A trial group will be comprised of 60 trauma patients and allocated into four groups of 15 patients each consisting of controls (saline-placebo) levamisole; vitamin A; and levamisole-vitamin A treated. The study will be performed in a double blind fashion with treatment being designated by random fashion derived by random number generation. All drugs will be dispensed in a suitable blinded fashion from the pharmacy. Therapy will begin by injecting immediately after necessary blood samples are taken for routine blood chemistries and removal of an additional 20cc of heparinized blood to be used for the immunological and microbial assays. Additional blood samples (20cc) will be taken on the following days; 3-5, 10-12, and 18-22 in order to monitor the immunological and microbial status of each patient. Only patients between 10 to 65 years of age who are admitted to the Trauma Unit between 2400 and 1200 will be included in this study. The time limitations are imposed due to the time required to perform the various in vitro assays. Blood samples obtained before 0630 will be refrigerated. All testing will be performed on the same day as the blood is drawn. Since this study will be comprised of military, civilian, individuals under the legal age of consent and adults not competent to give informed consent, appropriate consent forms will be accomplished.

Progress:

Due to long-term TDY OCONUS and subsequent reassignment to another institution of principal investigator, no patients were entered and the study has been terminated.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/19 Status: Completed
Title:

Chemotherapeutic Agents as Irrigation Solutions to Prevent Peritoneal
Implantation of Transitional Cell Carcinoma

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT K.L. Hansberry, MC

Dept/Sec: Assoc Investigators
Key Words: CPT I.M. Thompson, MC
Carcinoma COL F. Diaz-Ball, MC

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results
Study Objective:

To determine if additional efficacy is achieved by peritoneal
irrigation with chemotherapeutic agents during open surgery for
transitional cell carcinoma to prevent implantation of tumor.

Technical Approach:

Mice were implanted with human tumors. Two control groups were
implanted with saline and water and one group with cisplatinum.

Progress:

Provided good protection. Presented at the Proc. James C. Kimbrough
Seminar 1984. Paper is being submitted to J Urology.

Detail Summary Sheet

Date: 1 Oct 84 Prot No: 84/23 Status: Completed
Title:

The Effects of Two Exercise Programs on the Health of a
Forty-Year-Old Male Population

Start Date: Dec 1983 Est Comp Date:
Principal Investigator: Facility:

CPT C.C. Bucko, MSC

Dept/Sec: Physical Therapy Assoc Investigators
Key Words:

Exercise

Accumulative MEDCASE Est Periodic
Cost OMA Cost: Review Results

Study Objective:

To compare the effects of two ongoing physical training programs for
a forty-year-old male population.

Technical Approach:

A class of the USASMA will be selected as the study group. Those
failing the usual over-forty year old physical exam will be excluded
unless subsequently medically cleared by a cardiologist. Each class
contains approximately two hundred fifty students.

The class will be divided into two groups by a random number
method. The group participating in the exercise physiology based
program will be identified as the experimental group and the other
as the control group.

All subjects will take the standard US Army physical readiness exam
on the same morning. In addition, each individual's skin fold
measurements will be taken by a trained technician and his percent
body fat calculated. Hamstring flexibility for each individual will
also be determined by a standard method.

The experimental group will receive the ongoing instruction in how
to maintain their heart rate at 70% of maximum during exercise.
They will also be instructed in proper stretching techniques,
methods to improve pushup and setup strength, and effects of
exercise on body fat reduction.

Both groups will be allowed to train on their own for four months. Both will be retested and remeasured as indicated. During testing the testers will be unaware of the subject's group affiliation. The subjects will be assigned to test groups at random to eliminate bias.

Changes in percent body fat, flexibility, pushups, situps, and time to run two miles will be calculated from the test data. Significant differences between groups will be tested by comparing these changes with a Student's t-test.

Progress:

A manuscript has been submitted for publication.

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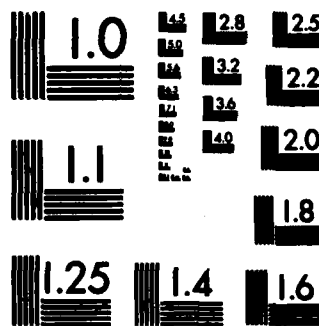
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